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ACTIVATED ELECTROENCEPHALOGRAPHY

I. CHARLES KAUFMAN, M.D.
BOSTON
CURTIS MARSHALL, M.D.
CHICAGO
AND
A. EARL WALKER, M.D.
BALTIMORE
With the Technical Assistance of
ELIZABETH M. BERESFORD, B.A., and GEORGE HOWE, B.S.

IN CASES of idiopathic epilepsy electroencephalographic abnormalities are commonly present, in the form of generalized dysrhythmias.[1] In a series of 240 cases of post-traumatic epilepsy these abnormalities were encountered in only 9.8 per cent, although foci of slow waves, probably due to the localized cerebral injury, were present in 77.7 per cent of the cases in which examination was made one to three years after injury.[2]

Accurate localization of the area of the cerebral cortex giving rise to the convulsive manifestation in post-traumatic epilepsy is necessary for surgical treatment of the condition. Since it seemed possible that an epileptogenic focus might be more susceptible to a convulsant drug than normal cerebral cortex, an attempt was made to activate the focus selectively by altering the chemistry of the blood. By using electroencephalographic recording to determine the activation before clinical manifestations appeared, it was hoped that the focus might be located without inducing a generalized seizure.

TECHNICS

The observations were made on a group of patients with post-traumatic epilepsy admitted to Cushing General Hospital for special study and on a small number of nonepileptic patients with cerebral wounds. The epileptic group consisted of patients who because of failure to respond to medical management were being considered for surgical therapy.

The work described in this paper was performed while the authors were assigned to Cushing General Hospital, Framingham, Mass.

1. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: The Electroencephalogram in Diagnosis and in Localization of Epileptic Seizures, Arch. Neurol. & Psychiat. **36**:1225 (Dec.) 1936. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Electroencephalographic Classification of Epileptic Patients and Control Subjects, ibid. **50**:111 (Aug.) 1943.

2. Walker, A. E.: Problems in Post-traumatic Epilepsy, read at the annual meeting of the American Psychiatric Association, Chicago, May 1945.

The electroencephalograms were made from electrodes placed conventionally on the scalp, with additional electrodes about the site of the healed wound or cranial defect and at least one electrode in a comparable position on the opposite side of the head. For "monopolar" recording an electrode attached to the ipsilateral ear was used as a common lead. The electroencephalograph was a four channel machine operating into an ink writer. In some cases two four channel machines were used simultaneously, the leads to the second machine being arranged for push-pull ("bipolar") recording from electrodes about the site of injury.

METHODS OF ACTIVATION

HYPERVENTILATION

It is well known that alterations of the acid-base equilibrium of the blood will increase or diminish the likelihood of convulsive seizures.[3] The usual technic of hyperventilation induces electroencephalographic changes in 20 to 35 per cent of epileptic patients, but determination of the actual change in the carbon dioxide content and the p_H of the cortical cells is a difficult, if not impossible, feat. Measurement of the respiratory exchange was attempted but was found unsatisfactory, owing to the difficulty of having the patient overventilate at a given rate and depth. The technic as employed by Davis and Wallace[4] was found to be too exacting for epileptic patients with neurologic disorders. In a group of 7 patients, all of whom seemed willing to cooperate, an attempt was made to obtain standard hyperventilation at a rate of 15 cycles per minute, each cycle representing an exchange of 20 cc. of air per pound of body weight. Kymographic recording of the respiratory exchange showed that individual patients achieved from 40 to 112 per cent of the standard. One patient (breathing 14.2 cc. of air per pound of body weight fifteen times a minute) had a jacksonian convulsion during the hyperventilation; the others did not have significant alterations in the electroencephalograms. Hyperventilation did not seem to be a consistent, satisfactory method for activating an epileptic focus.

HYDRATION

Hydration has been suggested as a technic for inducing convulsive phenomena in persons subject to epilepsy.[5] While clinical convulsions may be induced with this method in 25 to 40 per cent of such persons, it is a difficult procedure to control quantitatively. To 1 patient 1,000

3. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Electroencephalographic Response to Overventilation and Its Relation to Age, J. Pediat. **23**:497, 1943. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: Effect on the Electroencephalogram of Drugs and Conditions Which Influence Seizures, Arch. Neurol. & Psychiat. **36**:1236 (Dec.) 1936.

4. Davis, H., and Wallace, W. M.: Factors Affecting Changes Produced in Electroencephalogram by Standardized Hyperventilation, Arch. Neurol. & Psychiat. **47**:606 (April) 1942.

5. McQuarrie, I.: Epilepsy in Children: The Relationship of Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38**:451 (Sept.) 1929.

cc. of isotonic solution of sodium chloride was given intravenously over a period of ninety minutes, without any change in the electroencephalogram. In a series of 8 patients, 4 of whom had post-traumatic epilepsy and 4 post-traumatic encephalopathy without seizures, the hydration test, as described by Penfield and Erickson,[6] was carried out after anticonvulsant drugs had been withdrawn for a few days. The procedure is as follows: 1. Fluid is forced by mouth up to 3,000 to 6,000 cc. per day, an attempt being made to give equal amounts in each six hour period. 2. Pitressin, 0.5 cc., is injected intramuscularly every two hours during the procedure. 3. A diet containing considerable amounts of carbohydrate in various forms is given.

Under this regimen, all but 1 of the epileptic patients suffered such severe nausea and vomiting within twenty-four hours that the test had to be discontinued. Gains in weight of from 1.5 to 5.5 pounds (0.6 to 2.5 Kg.) were noted. No patient showed electroencephalographic changes, although 1 had a generalized seizure two hours after the test. In the group of nonconvulsive patients the gastrointestinal disturbances did not occur, but none of the patients had electroencephalographic alterations. It seemed inadvisable to use the procedure routinely, although it was obvious that the epileptic group reacted differently to the test than did the nonepileptic group.

ALCOHOL

Clinical experience has shown that seizures are prone to occur a day or two after an epileptic patient has indulged in alcoholic beverages.[7] In view of this fact, electroencephalograms were made on a series of 16 patients, 12 of whom were epileptic, during, immediately after and at intervals up to seventy-two hours after the rapid intravenous administration (2 to 3 min.) of 40 to 150 cc. of 10 per cent alcohol. In 4 instances alcohol levels in the blood were found to range from 100 to 150 mg. per one hundred cubic centimeters. In the nonepileptic group no alterations were noted in the electroencephalograms. In the epileptic group the alpha rhythm became more prominent and the amplitude of the previous abnormal activity decreased. All patients showed clinical evidence of alcoholic intoxication, although none was unable to walk.

TRIMETHADIONE

It has been noted that some patients being treated with trimethadione ("tridione") for petit mal have exhibited grand mal attacks.[8] For

6. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization, Springfield, Ill., Charles C Thomas, Publisher, 1941.

7. Lennox, W. G.: Alcohol and Epilepsy, Quart. J. Stud. on Alcohol **2**:1, 1941.

8. Lennox, W. G.: The Petit Mal Epilepsies: Their Treatment with Tridione, J. A. M. A. **129**:1069 (Dec. 15) 1945.

this reason, 18 patients with post-traumatic epilepsy were given trimethadione intravenously in doses of 50 to 500 mg. on a total of twenty-six occasions. Of the 18 patients, 12 had been given 500 mg. intravenously on at least one occasion. In no instance was there any noticeable effect on the electroencephalogram, but 1 patient, approximately thirty minutes after receiving the drug and after the electroencephalographic recording had been completed, had a focal epileptic attack, which did not become generalized.

ELECTRIC SHOCK

Because electric shock has proved to be such a simple and relatively innocuous convulsant agent, it was used in a group of 11 patients with post-traumatic epilepsy. Seven patients were given 200 milliamperes for 0.05 to 0.15 second, using a 60 cycle sine wave current. They presented only a startle reaction or mild tonic spasm at the instant of application of the stimulus. Four patients received 2 to 5 milliamperes of square wave, pulsating direct current for two to three seconds and felt only a sensation of warmness. The electroencephalograph was turned off just before the shock and on again immediately afterward. In no instance was there significant alteration in the electroencephalogram five seconds after the stimulus.

PENICILLIN

In view of the fact that penicillin has been shown to have a convulsant effect when applied to the cerebral cortex,[9] 100,000 units of the drug was given intravenously to a series of 5 patients, 4 of whom had organic disease of the brain, and the electroencephalographic record followed for thirty-five to fifty minutes. In no instance was any change noted in the record.

SODIUM CYANIDE

Because the cytochrome oxidase system[10] is impaired in patients with advanced dementia paralytica, in whom convulsive manifestations are common, and because cyanide is a specific poison for these enzymes, it was thought advisable to determine the effect of cyanide[11] on the patient with post-traumatic epilepsy. In a series of 17 patients, 14 of whom had seizures, a 2 per cent solution of sodium cyanide was administered intravenously. Three patients were given 0.3 mg. and the rest

9. Walker, A. E., and Johnson, H. C.: Penicillin in Neurology, Springfield, Ill., Charles C Thomas, Publisher, 1946.

10. Hadidian, Z., and Hoagland, H.: Chemical Pacemakers: I. Catalytic Brain Iron; II. Activation Energies of Chemical Pacemakers, J. Gen. Physiol. **23**:81, 1939.

11. Rubin, M. A., and Freeman, H.: The Influence of Cyanide on Brain Potentials in Man, J. Neurophysiol. **1**:527, 1938.

0.4 mg., per kilogram of body weight. Of the first group, 1 patient had no clinical or electroencephalographic reaction. In all the other patients a respiratory gasp occurred eight to twenty seconds after the injection, and a progressive slowing of the predominant activity appeared in their electroencephalograms (fig. 1). For example, in 1 patient the gasp occurred twenty seconds after the injection into the antecubital vein. Five seconds later the predominant rhythm in all leads was 8 cycles per second; five seconds later, 6 cycles per second, and eight seconds later, 2 cycles per second. Fifty seconds after the injection, widespread muscular twitching occurred throughout the body. Within seventy seconds after inhalation of 2 ampules (0.4 cc. each) of amyl

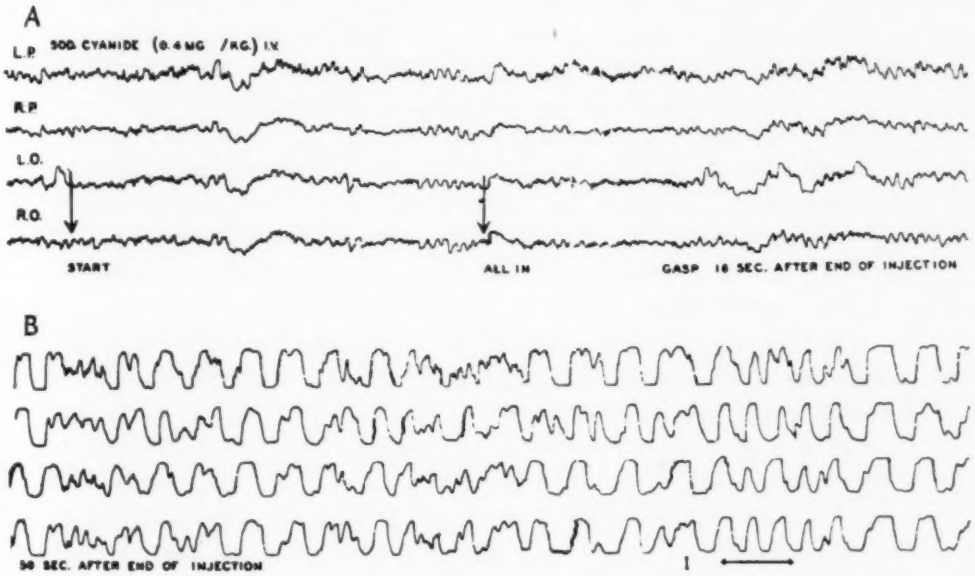

Fig. 1.—Records showing the effect on the electroencephalogram of sodium cyanide (0.4 mg. per kilogram of body weight) given intravenously. *A* is the control record, taken at beginning of the injection; *B*, the record taken fifty seconds after the injection, showing the generalized slow high voltage waves. *L.P.* indicates leads from the left parietal region and the left ear; *R.P.*, leads from the right parietal region and the right ear; *L.O.*, leads from the left occipital region and the left ear; *R. O.*, leads from the right occipital region and the right ear.

The vertical line at the base indicates a calibration of 50 microvolts; the horizontal line, an interval of one second.

nitrite, the slow waves had disappeared from the electroencephalogram. The slow waves were unrelated to the site of injury or to the site of electroencephalographic abnormality. In some cases the head and eyes turned to one side without constant relation to the site of injury. Occasionally opisthotonos developed. The reaction to the cyanide was the same in the nonepileptic as in the epileptic group.

ACETYLCHOLINE

It has been suggested that acetylcholine may be related to epileptic states.[12] A series of 18 patients, 15 of whom were epileptic, were given 100 to 300 mg. of acetylcholine chloride in aqueous solution at rates of injection varying from 20 to 60 mg. per minute. No change in the electroencephalogram was noted in any patient except for a decrease in amplitude of the waves for two minutes after the injection in 1 instance. The patients experienced a feeling of warmth and occasionally coughed, but had no other clinical manifestation related to the injection.

METRAZOL

It has been known for some time that clinical seizures could be induced in patients subject to epileptic attacks with a smaller dose of metrazol than that needed to convulse normal persons.[13] Lennox suggested that small amounts of metrazol might induce electroencephalographic alterations without precipitating a clinical attack. We found that the intravenous administration of 1 cc. of a 10 per cent solution (100 mg.) of the drug induced no clinical or electroencephalographic manifestations. Nor was the intravenous injection of 1.5 cc. of the metrazol solution more effective, but 2 cc. induced abnormalities in the electroencephalogram in a certain percentage of subjects. The technic was then standardized.

Metrazol, usually 2 cc. of a 10 per cent solution (200 mg.), was injected as rapidly as possible into the antecubital vein while an electroencephalogram was being recorded. The needle was left in place, and as soon as alterations were seen in the tracing, usually within thirty to sixty seconds, a solution of phenobarbital sodium (0.26 Gm.) was administered intravenously in an attempt to prevent the development of clinical convulsions. In a group of patients the metrazol was given by intramuscular administration, 6 mg. per kilogram of body weight being injected into the deltoid muscle. Phenobarbital sodium was given intravenously or intramuscularly as soon as changes were seen in the electroencephalogram, usually three to four minutes after the metrazol had been given.

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12. Brenner, C., and Merritt, H. H.: Effect of Certain Choline Derivatives on Electrical Activity of the Cortex, Arch. Neurol. & Psychiat. **48**:382 (Sept.) 1942. Williams, D., and Sweet, W. H.: Effect of Choline-Like Substances on Cerebral Electrical Discharges in Epilepsy, J. Neurol. & Psychiat. **4**:32, 1941. Forster, M., and McCarter, R. H.: Changes in Electrical Activity of the Cortex Due to Application of Acetylcholine, ibid. **54**:71 (July) 1945.

13. Langelüddeke, A.: Die diagnostische Bedeutung experimentell erzeugter Krämpfe, Deutsche med. Wchnschr. **62**:1588, 1936. Schönmehl: Provokation von epileptischen Krampfanfällen, Versuche und Ausblick, München. med. Wchnschr. **83**:721, 1936.

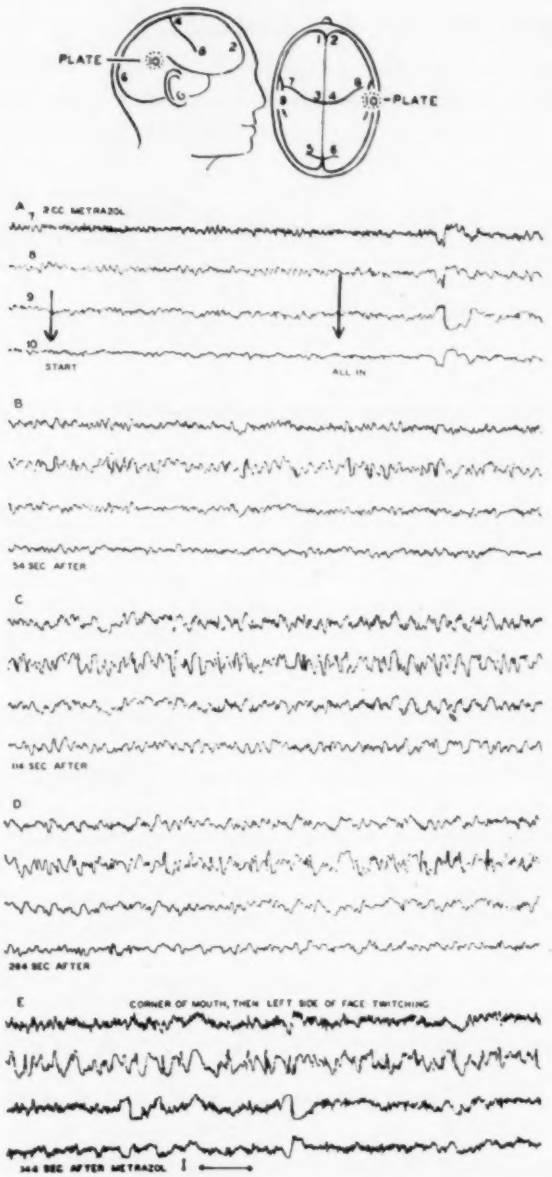


Fig. 2.—Electroencephalograms of a patient with post-traumatic epilepsy, showing activation of a focus by 2 cc. of a 10 per cent solution of metrazol given intravenously (*A*). Fifty-four seconds after the injection, high voltage 5 per second waves appeared in the tracing from the right inferior central region, whereas the activity in the other areas was little changed (*B*). Approximately two minutes after the injection all leads showed increased high amplitude activity, most pronounced in the left inferior central region (*C*). The general cortical activity became more irregular (*D*). Three hundred and forty-four seconds after the injection the spiky activity from the left inferior central region was more pronounced and twitching appeared (*E*).

The vertical line at the base indicates a calibration of 50 microvolts; the horizontal line, an interval of one second.

The results of activation with metrazol may be divided into electroencephalographic and clinical manifestations.

Electroencephalographic Changes.—Although in most instances slight alterations were present in the electroencephalograms from all parts of the head, in the majority of patients the changes were predominantly

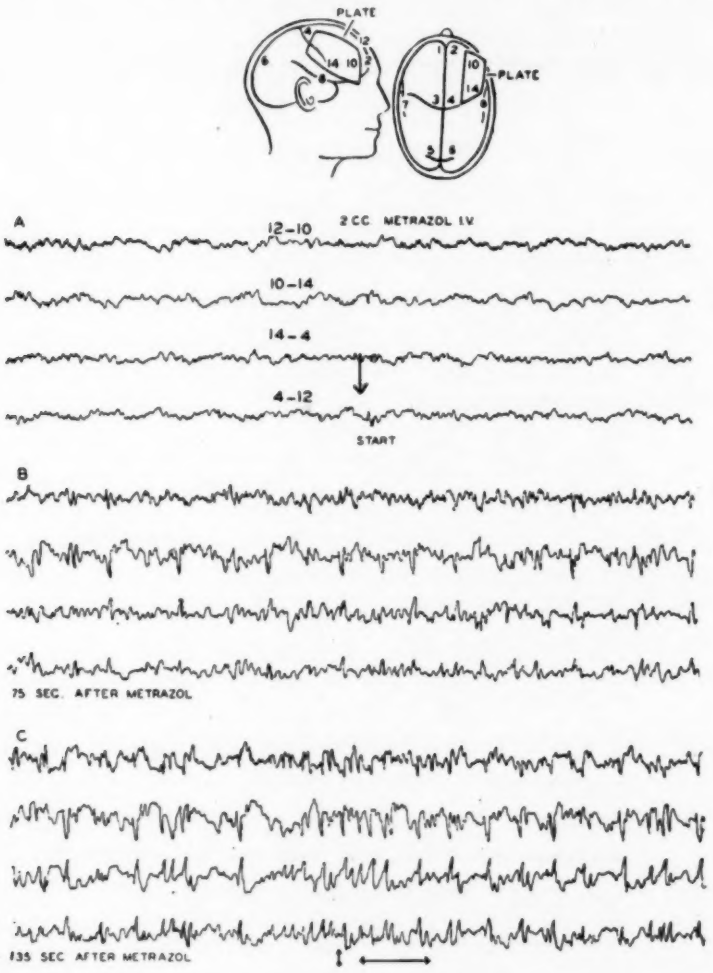
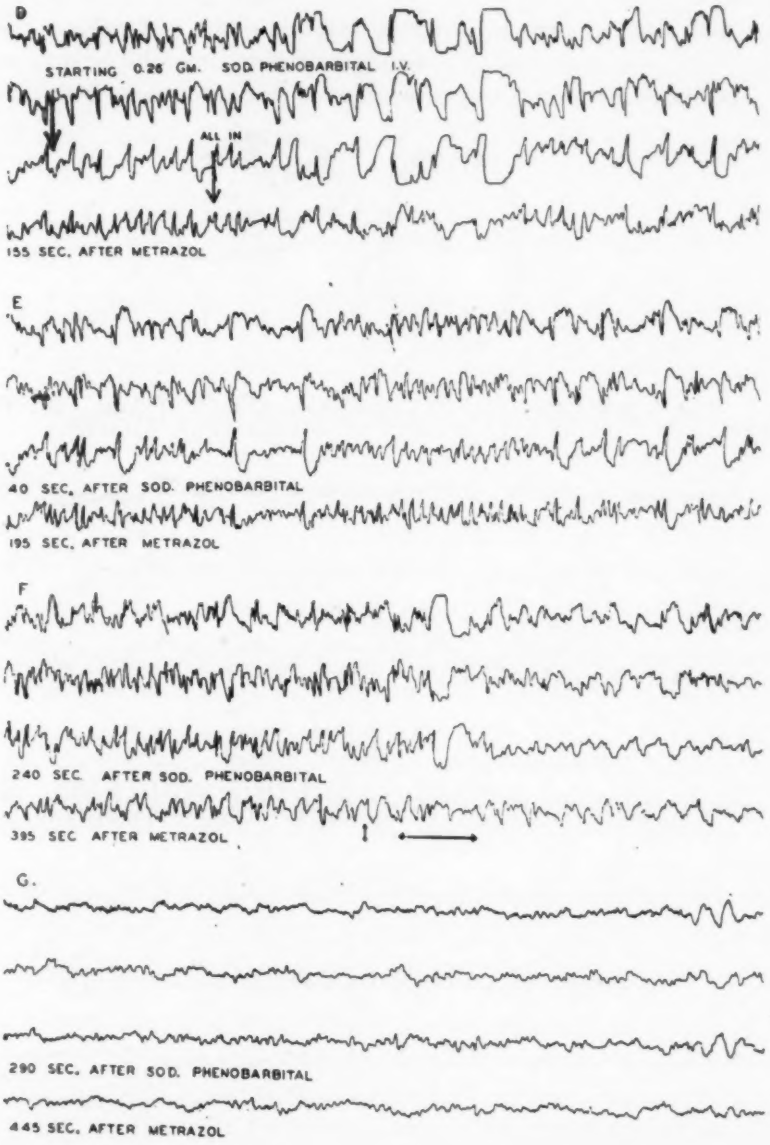


Fig. 3.—Electroencephalograms taken during activation with metrazol in a patient with post-traumatic epilepsy. The electrodes were placed on the scalp about a plate in the right frontal region, and the leads were arranged for push-pull recording.

(*A*) The record was taken during the intravenous administration of 2 cc. of a 10 per cent solution of metrazol (200 mg.); (*B*) seventy-five seconds after injection, spiking was seen in all records, but was most pronounced and out of phase in the tracings from electrode *14;* (*C*) one hundred and thirty-five seconds after the administration of metrazol, the spikes were of greater amplitude.

or solely in the tracings from one region (fig. 2). Such alterations are referred to as localized electroencephalographic alterations and might

take the form of slow waves or humps having a frequency less than the alpha rhythm, or of spikes, either single or multiple (fig. 3), at times occurring rhythmically, giving the pattern a localized electroencephalo-



(*D*) One hundred and fifty-five seconds after the injection, the spiky activity was still pronounced. Intravenous administration of phenobarbital sodium (0.27 Gm.) decreased the amplitude of the abnormal activity, as shown in the succeeding records, taken forty seconds (*E*), two hundred and forty seconds (*F*) and two hundred and ninety seconds (*G*) after the administration of the anticonvulsant drug. On the basis of this activated electroencephalogram, the abnormal focus was considered to lie beneath point *14*.

The short vertical sign at the base represents a calibration of the electroencephalograph for 50 microvolts; the horizontal line, an interval of one second.

graphic seizure (figs. 4 and 5). These abnormalities, if present before activation, were usually aggravated by the metrazol. Such localized electroencephalographic alterations occurred in 60 per cent of the 97 patients tested.

In a smaller number of patients (10 per cent) generalized electroencephalographic alterations consisting of single or multiple slow waves or spikes were present simultaneously in tracings made from several

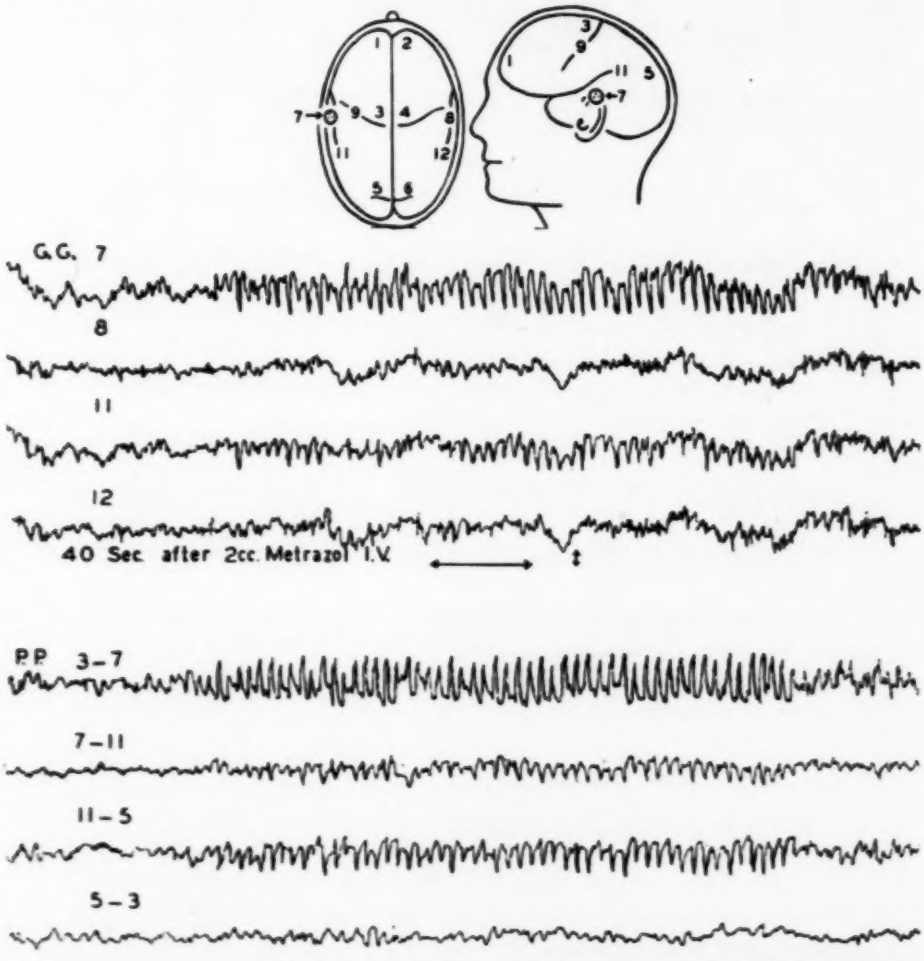


Fig. 4.—Electroencephalograms showing a predominant localized electroencephalographic seizure following the intravenous injection of 2 cc. of a 10 per cent solution of metrazol in a patient with post-traumatic epilepsy due to a penetrating wound in the left temporal region. All eight tracings are simultaneous recordings; the upper four being "monopolar" electroencephalograms from comparable areas of the two sides of the head and the lower four being push-pull recordings from about the cranial defect. The focus lies under point 7, the spiky waves having a higher amplitude and the push-pull recording showing out-of-phase activity from that region.

The vertical arrow under the first four tracings indicates a calibration of 50 microvolts; the horizontal arrow, an interval of one second.

parts of both sides of the head. In some instances the waves and spikes occurred rhythmically and simultaneously in all parts of the head from which recordings were taken, giving the pattern of a generalized electroencephalographic seizure (fig. 6).

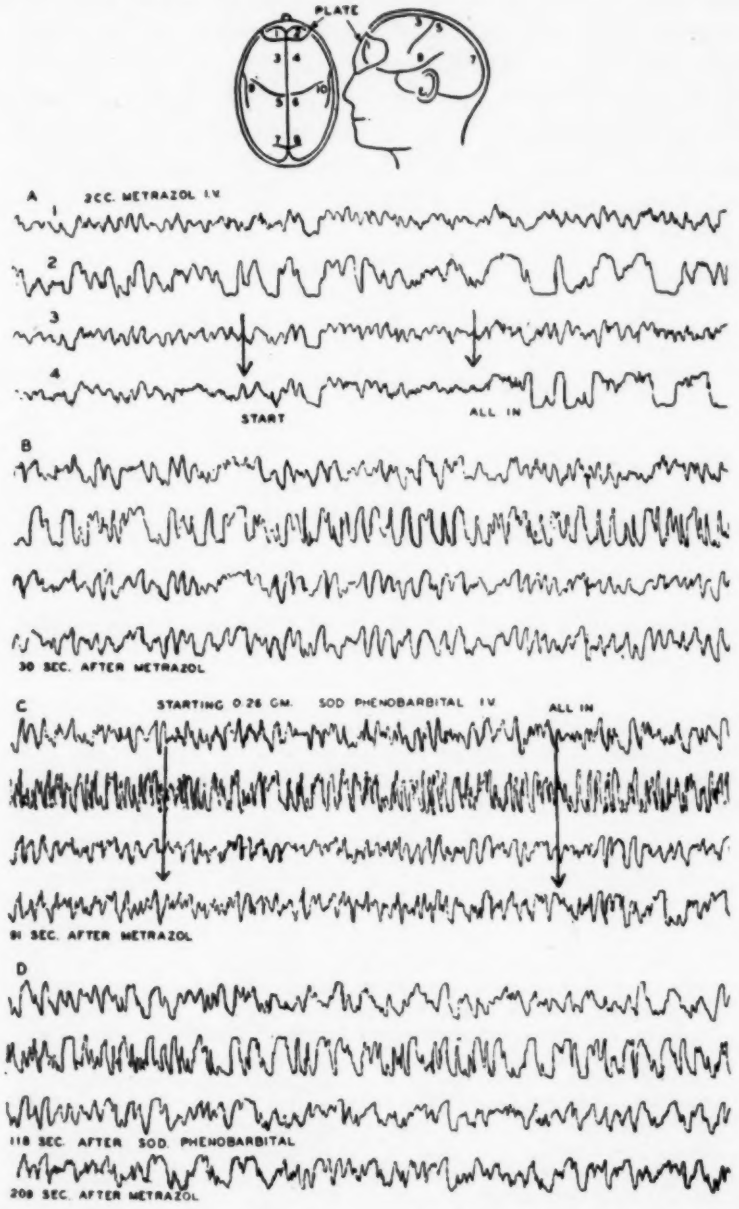


Fig. 5.—Activated electroencephalograms from a patient with post-traumatic epilepsy. A generalized slowing of the predominant rhythm occurred within thirty seconds after the injection of 2 cc. of a 10 per cent solution of metrazol, being most prominent in the second lead (*A* and *B*). Within a minute and a half of the injection the activity became faster and the waves sharper (*C*). The intravenous injection of 0.26 Gm. of phenobarbital sodium decreased the spiky fast activity (*D*).

Clinical Manifestations.—A small percentage of patients experienced sensory or motor phenomena such as they usually associated with their spontaneous seizures. In approximately one-half these patients the attack remained confined to one portion of the body and is referred to as a focal convulsion. In the remainder the attack began as or developed into a generalized seizure involving all parts of the body and being associated with loss of consciousness (table 1).

The seizures induced by metrazol had the characteristics of the patient's ordinary attacks. The fit was ushered in by the same aura, progressed in the usual order and had identical motor phenomena. The severity of the seizure was comparable to that of the spontaneous con-

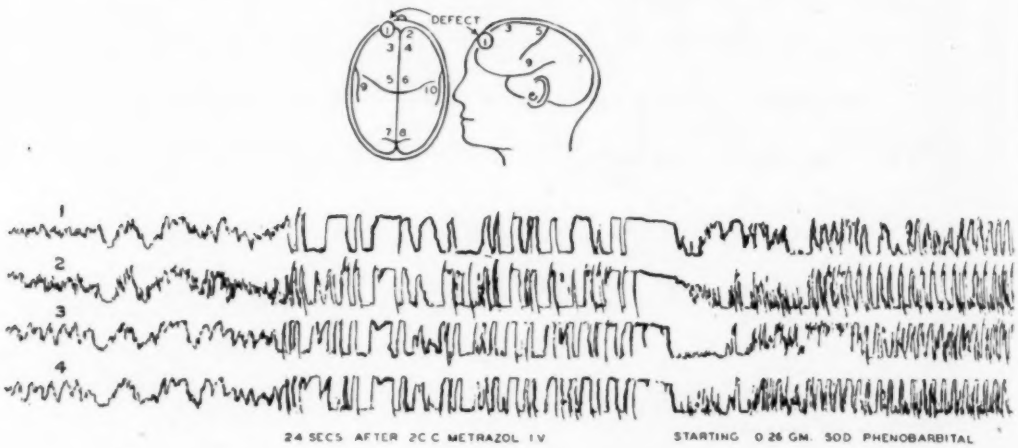


Fig. 6.—Electroencephalogram showing a generalized electroencephalographic seizure beginning practically simultaneously from the two frontal regions of the head after the intravenous injection of 2 cc. of a 10 per cent solution of metrazol in a patient with post-traumatic epilepsy. The leads are taken from the frontal region, as indicated, with the second electrode on the ear.

TABLE 1.—*Results of Metrazol Activation in Patients with Post-Traumatic Epilepsy*

	Number of Patients
Number of patients receiving metrazol activation *	97
Generalized electroencephalographic alterations	7
Localized electroencephalographic alterations	58
Localized and generalized electroencephalographic alterations	10
Localized slow waves	83
Localized spikes	31
Localized electroencephalographic seizure	18
Generalized slow waves	5
Generalized spikes	6
Generalized electroencephalographic seizure	6
Clinical focal convulsion	10
Clinical generalized convulsion	14

* In a number of patients activation with metrazol was carried out more than once (table 4), but in this table a positive result in any category is included only once for each patient, although he may have had a positive result on each of four tests. Accordingly, the figures are smaller for each phenomenon in this table than in table 4.

TABLE 2.—*Frequency and Number of Spontaneous Seizures and Incidence of Convulsions Induced by Activation with Metrazol*

	Number of Patients	Mean Weight of Patients, Lb.	Mean Number of Attacks	Mean Interval Between Attacks, Months	Mean Time Between Last Attack and EEG Examination, Months
Clinical convulsions...	19	162.2	5.7	2.0	2.4
No convulsions.....	19	152.1	9.7	0.9	1.8

TABLE 3.—*Results of Repeated Activation with Metrazol in Patients Without Primary Localizing Electroencephalographic Phenomena*

	Electroencephalographic Alterations						
First test.....	None			Generalized			Localized
	43			10			44
Second test.....	Generalized	None	Localized	None	Generalized	Localized	
	1	21	8	1	2	3	
Third test.....	Generalized	None	Localized	None	Generalized	Localized	
	0	5	0	1	0	1	
Fourth test.....		None					
		2					
Fifth test.....		None					
		2					

TABLE 4.—*Results of Repeated Activation with Metrazol* *

	Test No.											
	1			2			3		4		5	
	On†	Off†		On	Off		On	Off	On	Off	Off	
	IV	IV	IM	IV	IV	IM	IV	IV	IV	IV	IV	Total
Generalized electroencephalographic alteration.....	2	8	0	1	4	0	0	1	0	0	0	16
Localized electroencephalographic alteration.....	10	33	1	3	17	5	2	4	0	3	2	80
No electroencephalographic alteration...	9	30	4	9	25	3	3	6	1	1	3	94
Total.....	21	71	5	13	46	8	5	11	1	4	5	190
Generalized slow waves.....	2	1	0	0	2	0	0	0	..	0	0	5
Generalized spikes.....	1	4	0	0	0	0	0	1	..	0	0	6
Generalized electroencephalographic seizures.....	0	5	0	1	2	0	0	0	..	0	0	8
Localized slow waves.....	9	14	0	2	7	1	2	1	..	1	1	38
Localized spikes.....	3	13	1	2	7	4	1	2	..	3	2	38
Localized electroencephalographic seizures.....	1	11	0	1	6	1	0	1	..	0	0	21
Total.....	16	48	1	6	24	6	3	5	..	4	3	116
Clinical Phenomena												
Focal convulsions.....	0	5	0	0	4	0	0	1	0	0	0	10
Generalized convulsions.....	0	9	0	0	4	2	0	1	0	0	0	16

* IV means intravenous, IM intramuscular, administration.

† On indicates that the patient was receiving anticonvulsant medication at the time of the test; Off, that no medication had been received for at least three days prior to the examination.

vulsion. However, there was no relation between the frequency and number of attacks which the patient had had and their occurrence on activation with metrazol (table 2).

Repeated Activation with Metrazol.—Because a single activation with metrazol gave positive localizing electroencephalographic changes in less than one-half the patients studied, reexaminations were made on a number of patients showing no such alterations in the primary examination (tables 3 and 4). Approximataely one-third this group had localized electroencephalographic alterations on the second test. Reexamination was made also of a number of patients who had focal electroencephalographic alterations on the first test. Although the majority again had focal abnormalities, some showed no electroencephalographic alterations on the second activation. It must be concluded, then, that focal activation is not consistently found in the same patient on repeated examinations. However, when activated, the focus appears to be at the same locus. It would, then, seem worth while to reexamine by metrazol activation patients who do not show a focus on the first examination.

Activation by Intravenous and Intramuscular Injection of Metrazol.—To a group of 11 patients, 6 mg. of metrazol per kilogram of body weight was administered intramuscularly. Only 1 patient had a clinical generalized seizure, and only 2 showed localizing electroencephalographic changes (fig. 7). Nine of the 11 patients were given 2 cc. of a 10 per cent solution of metrazol intravenously, and all showed focal electroencephalographic alterations. It would seem, then, that while the intramuscular method of administration of metrazol may be less likely to produce clinical seizures, it is much less efficient in activating an epileptogenic focus.

Effect of Anticonvulsant Medication on Activation with Metrazol.—Routinely, patients were given no anticonvulsant medicament for three days before activated electroencephalographic recording. However, in a group of patients, activation with metrazol was carried out without preliminary elimination of drug therapy. In a series of 40 patients receiving such activations, 3 (7.5 per cent) showed generalized electroencephalographic changes and 15 (37.5 per cent) localized alterations. This is a definitely lower incidence of activation than that in the group not receiving anticonvulsant medication. However, none of the patients in this group had clinical convulsions. It may prove advisable to carry out activation with metrazol while the patient is receiving anticonvulsant medication in order to lessen the risk of inducing an overt convulsion.

Activation with Metrazol as a Prognostic Guide.—As a patient's attacks became controlled by medication, it was hypothesized that tolerance to metrazol, as determined by electroencephalographic and clinical

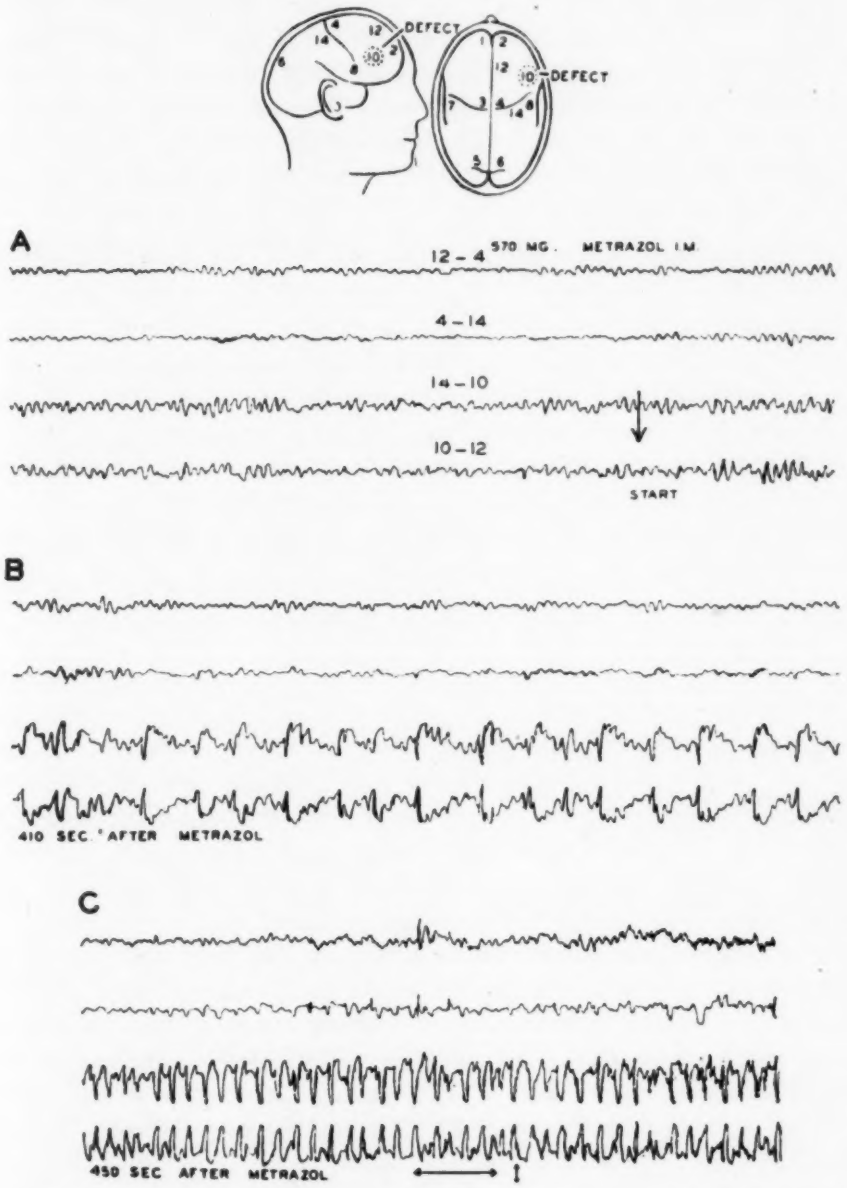


Fig. 7.—Electroencephalograms showing push-pull recording about the cranial defect of a patient with post-traumatic epilepsy (*A*). At the arrow, 570 mg. of metrazol was injected into the right deltoid muscle. Seven minutes later the cortical activity, as recorded by electrodes over and above the defect, showed rhythmic spikes (1 to 2 cycles per second), being out of phase in electrode *10* (*B*). Seven and one-half minutes after the injection the spikes had a 5 per second frequency and at times had small humps or domes between them, resembling to some extent the hump and spike pattern of petit mal (*C*). Even when the activity was very prominent in the tracing from the electrodes near the defect, the electroencephalogram from the electrodes in the paracentral region showed only slight alterations.

The vertical line at the base of the tracings represents a calibration of 50 microvolts; the horizontal line, an interval of one second.

responses to activation, might be increased. However, this did not appear to be the case, for patients who had had no attacks for six months had both electroencephalographic and clinical abnormalities on activation with metrazol, whereas some patients having attacks every two to three weeks showed no electroencephalographic or clinical reaction (table 2). The activation cannot, then, be considered an accurate prognostic or therapeutic guide.

Correlation of Electroencephalographic Foci and Epileptogenic Foci Observed at Operation.—In 39 of the patients the cerebral cortex was explored because of the uncontrollable epilepsy. At the time of cortical exploration either metrazol or electrical activation or both were carried out. In all instances in which a focus was demonstrated by the activated electroencephalographic method the locus of the focus was confirmed at the time of operation. Several technics were employed to remove the foci, with or without the scar. While the results of operation have been satisfactory so far, it is too soon to make a definite statement regarding the results of the procedure.

COMMENT

The value of actually witnessing the typical attack of an epileptic patient has been recognized for many years. But only recently have methods for inducing such attacks been seriously considered. In general, the technics of hyperventilation and hydration have not been very successful, either because of the low incidence of induced attacks or because of the unpredictable time of occurrence. The attack, when produced, however, has been typical of the patient's usual seizure. The use of metrazol to produce convulsions, suggested first by von Meduna,[14] has the distinct advantage that the attack may be produced at the time the patient is under observation. Penfield and Erickson [6] stated that the test is of doubtful value in cases of epilepsy, since it leads to seizures in a high percentage of nonepileptic as well as epileptic patients. This disadvantage is not serious if one is using the test to determine the pattern of the seizure in patients known to have convulsions. Penfield and Erickson admitted that the test "would be useful only if it is shown that small doses faithfully reproduce the patient's spontaneous attacks." [15] This similarity we, as well as others, have demonstrated, although we have no doubt that if too large doses are given the pattern of a focal attack may be obscured by the rapid onset of a generalized attack.

14. von Meduna, L.: Versuche über die biologische Beeinflussung des Ablaufes der Schizophrenia: I. Campher- und Cardiozol Krämpfe, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:235, 1935.

15. Penfield and Erickson,[6] p. 458.

Perhaps the slow intravenous injection of a more dilute solution [16] might be advisable in such circumstances.

By recording an electroencephalogram during the actual injection of the convulsant drug, the likelihood of a generalized seizure is decreased, since as soon as abnormalities become apparent an anticonvulsant drug may be given intravenously. We believe that the clinical and electroencephalographic information gained more than compensates for the possible risk of inducing a convulsive seizure.

SUMMARY

In a series of 97 patients with post-traumatic epilepsy, an attempt was made to activate the epileptogenic focus by hyperventilation, hydration, electric shock, intravenous administration of alcohol, and injection of trimethadione, penicillin, acetylcholine chloride, sodium cyanide and metrazol.

Of these methods, the injection of metrazol proved to give satisfactory focal activation in approximately 44 per cent of the patients on the first test and in a much higher percentage on repeated testing.

Intravenous administration was more effective than intramuscular injections.

Clinical seizures occurred in approximately 14 per cent of patients, but not if anticonvulsant medication was given before the test.

The electroencephalographic alterations induced with metrazol included focal slow waves, spikes or, somewhat less frequently, the rhythmic discharge of a seizure. The same alterations were less commonly recorded from all parts of the head.

Activated electroencephalography appears to be a useful diagnostic aid in the understanding of the mechanisms involved in post-traumatic epilepsy.

80 East Concord Street, Boston.
950 East Fifty-Ninth Street, Chicago.

16. Dr. E. Ziskind, of Los Angeles, in discussing a paper by one of us (A. E. W.)[2] presented at the one hundred and second annual meeting of the American Psychiatric Association in May 1946, stated that he was using that technic to determine convulsive thresholds and that it rarely precipitated a generalized convulsion.

FATAL CRYPTOGENIC NEUROPATHY

SAMUEL BROCK, M.D.
AND
CHARLES DAVISON, M.D.
NEW YORK

UNDER THE caption of "fatal cryptogenic neuropathy," we wish to put on record the clinical and pathologic observations in 3 cases in which the brunt of the disease was sustained by the peripheral nervous system (roots and nerves), though in 2 of the cases there were evidences of lesser involvement of other parts of the neuraxis. Use of the usual prefixes indicative of such higher involvement, to which the suffix "pathy" must needs be added, would lead to a compound and cumbersome title which would not emphasize the major implication of the peripheral nerves. However, we would not give the impression that we are describing a new disease, clinically or pathologically.

In the recent neurologic literature there are many well known references to special forms of neuritis or neuropathy the cause of which is unsettled. Thus, one may refer to the group of cases described by Guillain, Barré and Strohl in 1916,[1] and again by Guillain in 1936,[2] as well as to cases of acute febrile polyneuritis,[3] certain instances of acute febrile polyneuritis with facial diplegia[4] and a variety of other forms,[5] such as relapsing or recurrent polyneuritis and polyneuritis associated with hematoporphyrinuria. In connection with the "radiculoneuritis with acellular hyperalbuminosis of the cerebrospinal fiuid" which he

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Presented at a meeting of the New York Neurological Society, March 4, 1947.

From the Neuropathological Laboratory and the Neuropsychiatric Service of the Montefiore Hospital for Chronic Diseases, and the Neurological Department of Columbia University College of Physicians and Surgeons.

1. Guillain, G.; Barré, J. A., and Strohl, A.: Sur un syndrome de radiculonévrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire: Remarque sur les caractères et graphiques des réflexes tendineux, Bull. et mém. Soc. méd. d'hôp. de Paris **40**:1462, 1916.

2. Guillain, G.: Radiculoneuritis with Acellular Hyperalbuminosis of the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **36**:975 (Nov.) 1936.

3. Holmes, G.: Acute Febrile Polyneuritis, Brit. M. J. **2**:37, 1917.

4. Bradford, J. R.; Bashford, E. F., and Wilson, J. A.: Acute Infective Polyneuritis, Quart. J. Med. **12**:88, 1918. Forster, F. M.; Brown, M., and Merritt, H. H.: Polyneuritis with Facial Diplegia, New England J. Med. **225**:51, 1941.

5. Wilson, S. A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1940, vol. 1.

described, Guillain [2] stressed the cytoalbuminous dissociation and the favorable prognosis. He expressed the belief that the disease is of infectious origin, i. e., due to a neurotropic virus. Guillain [2] described the onset of the disease—sometimes abrupt—the progressive areflexic flaccid paralysis, the mild to moderate muscular wasting, the slight objective sensory defects, the neuritic pains in the limbs and the occasional involvement of the cranial nerves. Despite the fact that over thirty years have passed since the French called attention to the clinical picture, the cause of the disease has escaped detection.

In reporting the following 3 fatal cases, in 2 of which there were repeated evidences of increased protein in the spinal fluid, we would stress the fact that our cases of fatal "neuritis or neuropathy" were characterized by considerable variation in duration and symptoms. Despite a similarity in neuropathologic changes, it is not at all certain that we are dealing with a disease due to a single cause.

REPORT OF CASES

CASE 1.—E. W., a single woman aged 26, a stenographer, entered the Neurological Institute of New York on May 26, 1936 and was discharged to the Montefiore Hospital on Nov. 16, 1936. She died on Jan. 7, 1937.

She had a past history of measles and scarlet fever and of acute nephritis following a "cold" in 1932; the last disease was associated with edema of the ankles and the eyelids.

The patient's sister, M. W., aged 22, born of the union of the patient's father and her mother's sister, was admitted to the Neurological Institute of New York on Aug. 9, 1935. She complained of progressive loss of vision, occasional dizzy spells, tingling sensations, slight numbness and stiffness of the fingers of the right hand and diplopia of two weeks' duration. The right pupil was slightly larger than the left; both reacted sluggishly to light; there were slight photophobia and generalized hyperreflexia. Ophthalmologic examination disclosed pallor of the temporal side of the left fundus. Examination of the spinal fluid disclosed 7 cells per cubic millimeter, a negative reaction for globulin, 24 mg. of protein per hundred cubic centimeters, a colloidal gold curve of 112211100 and a negative Wassermann reaction; the blood also gave a negative Wassermann reaction. The diagnosis was multiple sclerosis with retrobulbar neuritis.

E. W. became ill in March 1936. She noticed that her arms became unusually tired and her fingers stiff when typing. On April 13 her lower limbs seemed to drag because of weakness. Soon both lower limbs became weaker, the left being affected more than the right. On April 23 the right arm became weak. On April 28 the left arm was similarly affected. She could no longer walk. In typing she could use only either index finger.

She was admitted to the Neurological Institute on May 26, 1936. In June of the same year she became unable to feed herself. Toward the middle of that month she was able to move only one finger at a time. There was no history of fever, pain, headache, deafness, tinnitus or disturbance in vision. By June 8 the flaccid paralysis in the four limbs had become extreme and continued with little or no change over the subsequent months. Only the faintest flicker of movement at the left elbow (left biceps muscle) and slight movement of the left index finger were observed. The muscles of the neck, chest and abdomen seemed

relatively uninvolved. The innervations of the cranial nerves were normal. Sphincter action was unaffected. Muscular atrophy was noted in the interossei and in the anterior and posterior tibial groups in July 1936. Later in July there was diminished power in holding the head forward against resistance. No sensory defects were noted until late July, when vibratory sense was found to be diminished over the right tibia. The sensory defect disappeared in the next few months. In late July of 1936 blurring of the upper margins of the optic disks first appeared; this change in the disks progressed little, if any. In September 1936 striate hemorrhages were found above the papillae and the retinal vessels seemed more engorged. All the deep reflexes were missing except for an occasional response in the left pectoral and biceps muscles.

Because of the presence of infected tonsils, a tonsillectomy was performed on October 14.

On Nov. 5, 1936, the physical status was as follows: There were pallor of the nails, coldness of the extremities, slight cervical kyphosis and some tenderness and limitation of passive movement of the joints of the limbs, especially the elbows. Muscular atrophy was extreme in the lower extremities and slight in the upper extremities. She was able to use the muscles of the neck and the upper thoracic and lower lumbar regions, particularly on the left side; there were increased irritability and tenderness of the muscles of the upper extremities. Flaccid paralysis of all muscles of the limbs was noted; the scapular and the left pectoral and biceps muscles were paretic. There was generalized areflexia except for occasional responses in the left pectoral and biceps muscles. No gross sensory defects were noted. There were some blurring of the margins of the disks and slight evidence of old retinitis. The visual fields were normal. The left pupil was larger than the right; the corneal and gag reflexes were diminished. The tongue showed fibrillations, with slight deviation to the right. The cranial nerves were otherwise normal. The patient's mood tended to fluctuate between optimism and severe depression, with occasional episodes of increased irritability.

She was admitted to Montefiore Hospital on November 16. Neurologic examination then disclosed practically the same picture as that just described except that there was slight diminution of tactile sensation in both feet as compared with the rest of the body; pain and temperature sensations were diminished in both lower extremities below the knees and to a less extent in both hands. This diminution was somewhat patchy in its distribution, the patient occasionally calling "pinprick" dull in one area and sharp in an adjacent one. Vibratory sense was impaired, being absent in both feet, greatly diminished in both legs and slightly diminished as high up as the eighth thoracic dermatome. There was evidence of severe vasomotor disturbance in the hands and in the feet, which were cold, clammy and distinctly pale. There was profuse and continuous sweating on the palms and soles. There seemed to have been some astereognosis in both hands, but it was difficult to evaluate this because of the complete paralysis of the hands and fingers.

Sensory examination on November 27 disclosed vague sensory disturbances—hypalgesia and thermhypesthesia up to the tenth thoracic dermatome and loss in vibratory sensation in the lower extremities to about the knees.

In December 1936 the patient showed a tendency to gag on swallowing and difficulty in coughing. Atrophy of the muscles of the extremities became extreme, especially in the lower third of the thighs and in the hypothenar and thenar eminences. There were bilateral hand and foot drop and almost total areflexia. There were weakness of both trapezius and supraspinatus muscles and slight weakness of the sternocleidomastoid muscles. The abdominal reflexes were absent.

During her stay in the hospital the temperature, pulse and respiration were normal except terminally. Her blood pressure varied from 126 systolic and 80 diastolic to 140 systolic and 100 diastolic.

On November 21 reaction of degeneration was noted in most of the neuromuscular units. On December 7 the red glass test revealed weakness of the left internal rectus, the left superior and inferior rectus and the right superior and inferior rectus muscles. On Feb. 2, 1937 the patient began to complain of difficulty

Data on the Spinal Fluid (1936) *

Date	Cells	Globulin	Protein, Mg./100 Cc.	Sugar, Mg./100 Cc.	Chlorides	Colloidal Gold Curve	Wassermann Reaction, 0.2 to 2 Cc.
5/27	3	+++	243	56	680	.....	Negative
6/ 5	3	+	200	..	...	111122211	.....
6/ 9	5	+++	94	..	...	.....	.....
6/30	2	++	125	..	...	.....	.....
7/14	3	+++	125	..	...	111122111	Negative
7/18	3	+++	250	75	765	.....	.....
7/22	3	+++	250	62	710	.....	.....
8/ 4	3	+++	200	..	...	.....	.....
9/12	5	++	113	..	...	.....	.....
10/17	9	++	112	..	...	2222233311	.....
11/16	4	+++	146	75	750	.....	Negative

* There was no evidence of manometric block. The spinal fluid pressure measured from 90 to 200 mm.

in swallowing solid food; she salivated profusely and was cyanotic. Bronchopneumonia developed, and she died on February 7.

Laboratory Data.—The spinal fluid showed pronounced cytoalbuminous dissociation (table).

Repeated blood counts, chemical studies of the blood, serologic tests and urinalyses revealed nothing significant. The sedimentation rate was 18 mm. in one hour (September 1936). Special analyses for lead and arsenic gave results as follows:

Lead

Blood, Mg./100 Gm. Solids	Urine, Mg./1,000 Cc.	Feces, Mg./100 Gm.	Spinal Fluid
May 29.....1.2	September 5.....0.026	September 5.....0.0	June 9.....0.0
September 5.....1.1	September 8.....0.0	September 25.....0.58	
September 9.....0.0	September 25.....0.0	October 7.....2.5	
September 25.....0.85	October 7.....0.033	October 30.....1.05	
October 7.....2.4	October 30.....0.018	November 13.....2.6	
October 30.....1.2			
November 13.....1.54			

Arsenic

Blood, Mg./100 Gm.	Urine, Mg./100 Gm.	Feces, Mg./100 Gm.
May 29.....0.037	June 6.....0.425	September 9.....0.0
October 7.....0.0	September 8.....Trace	October 7.....0.022
	October 7.....0.0	

No lead was found in the rouge or lipstick used by the patient. Her face powder contained 4.1 mg. of lead per 1.1 Gm. of powder. Specimens of the cold and hot water taken from her home contained no lead.

Although the quantity of lead in the blood was high, the amount of urinary lead was not. Analyses for arsenic did not reveal an abnormal amount except in the urine on June 6. These heavy metals were not believed responsible for the clinical picture presented by the patient.

Roentgenograms of the spine and skull revealed nothing abnormal.

The blood serum contained 1.81 Gm. of albumin and 2.15 Gm. of globulin. The basal metabolic rate was + 3 per cent. Sweating tests showed no sweating below the umbilicus after one hour.

Treatment.—A variety of therapeutic measures were tried, to no avail. These included tonsillectomy (October 1936), intravenous injections of hypertonic solutions of dextrose and calcium carbonate, hyperthermia and a deleading regimen, i. e., institution of a low calcium, high phosphorus diet and administration of sodium thiosulfate by mouth. These measures accounted for the increase of lead in the excreta noted in the tabulation.

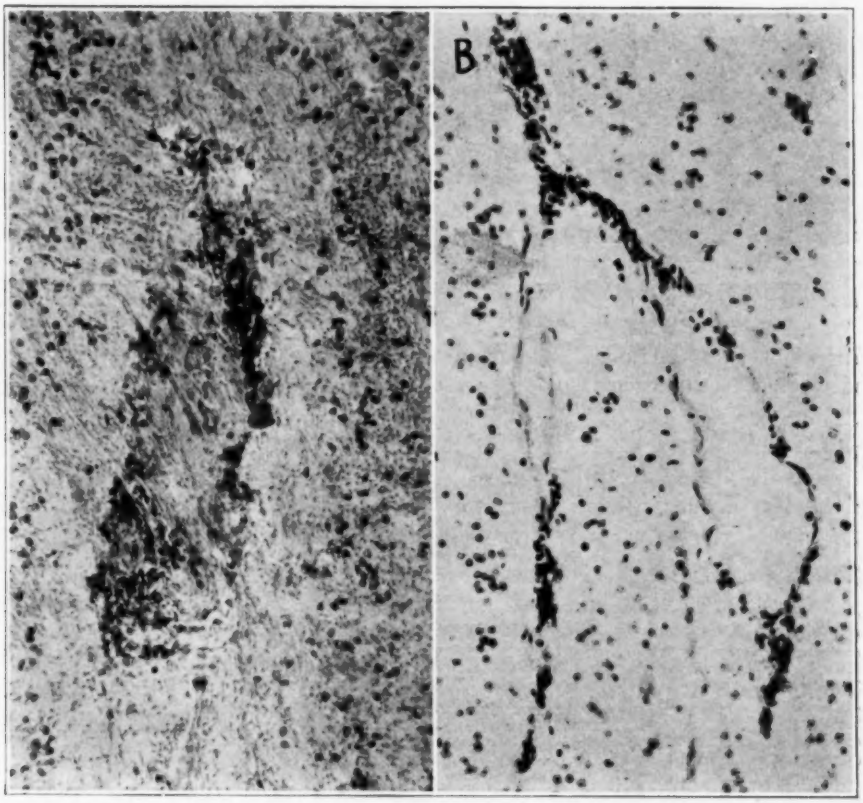

Fig. 1 (case 1).—*A*, iron deposits, few lymphocytes and area of destruction around the perivascular spaces in the cortex. *B*, inflammatory reaction in the hippocampus. Cresyl violet; × 100.

Autopsy.—Gross Examination: The pia-arachnoid of the brain, especially over the frontal convolutions, had a dull, opaque appearance. The pia stripped readily. The cranial nerves appeared normal. The vessels of the white matter were slightly prominent.

The spinal cord showed no gross abnormalities. Various regions of the cord, including the conus medullaris and the cauda equina, and sections from the brachial plexuses, the right lumbar plexus and the left sciatic nerve were embedded for further study.

Microscopic Examination: Sections from various cortical regions, the optic nerves, chiasm and tracts, and the diencephalon, pons, medulla oblongata, cerebellum and dentate nuclei were stained by the myelin sheath and cresyl violet methods. Frozen sections of the spinal cord were also stained with the Spielmeyer and sudan III methods. The peripheral nerves were stained for myelin sheaths and by the Marchi, sudan III and Bielschowsky methods.

Cortex: The cortical sections, especially from the frontal and hippocampal regions, disclosed edema of the pia-arachnoid, with slight proliferation of the

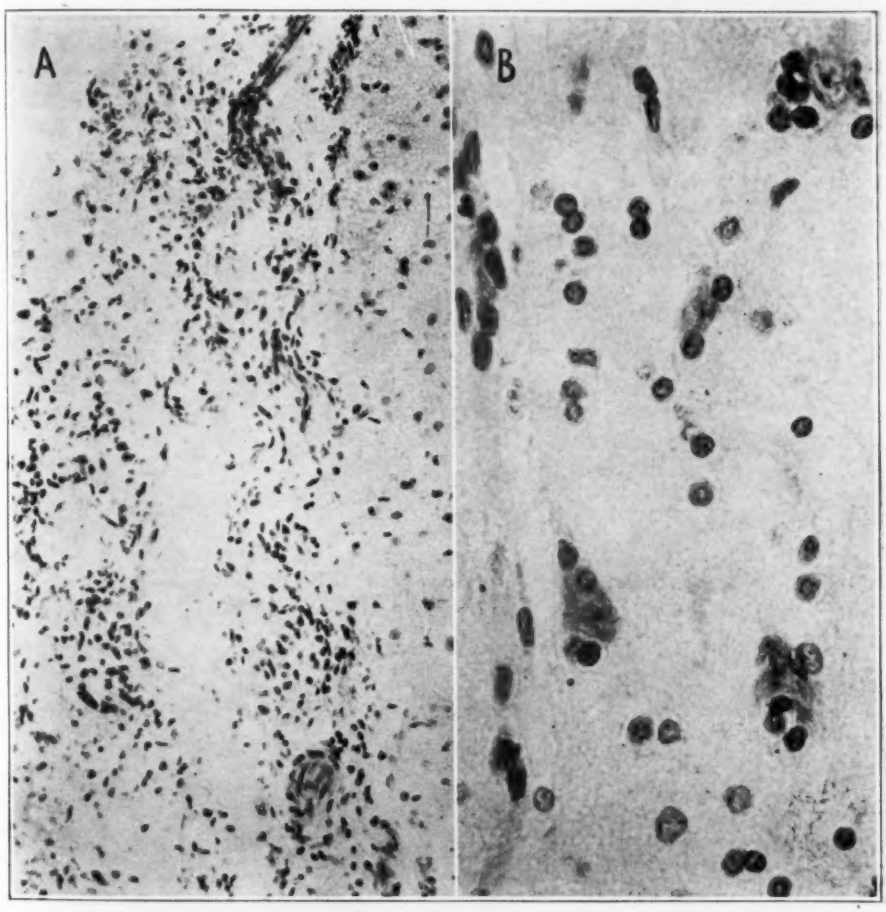

Fig. 2 (case 1).—*A*, meningitic reaction and extravasation of blood from the hippocampal area. *B*, neuronophagia and satellitosis of nerve cells of the hippocampus. Cresyl violet; × 400.

arachnoidal cells but no inflammatory reaction. There was no distortion in the arrangement of the cytoarchitectural layers of the cortex, but the perivascular spaces of the cortex and the white matter contained deposits of iron and a few lymphocytes (fig. 1 *A*). There were also small areas of devastation surrounding the vessels (fig. 1 *A*). A few hippocampal vessels contained occasional lymphocytes and plasma and endothelial cells (fig. 1 *B*). In one area the meninges of the hippocampus showed a slight inflammatory reaction, consisting of a few

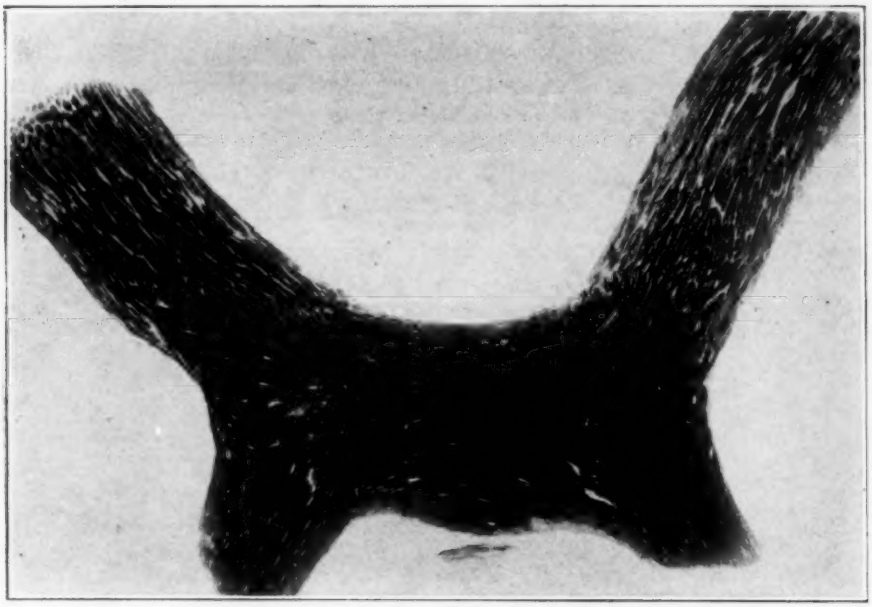

Fig. 3 (case 1).—Perivascular demyelination in the optic nerves.

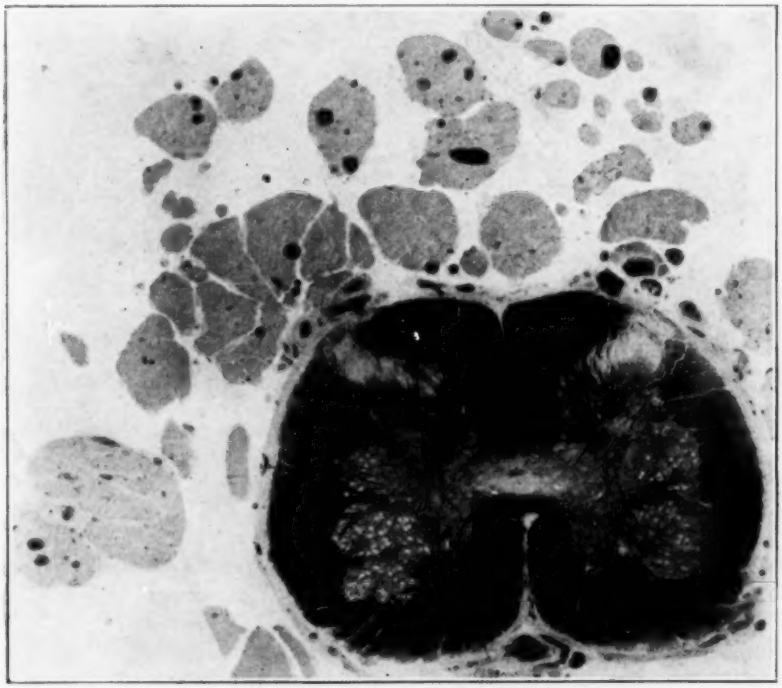

Fig. 4.—Severe demyelination of practically all the roots in the sacral region.

lymphocytes, pigmentary deposits, reticuloendothelial cells and extravasation of red blood cells (fig. 2 *A*). Some of the nerve cells near the perivascular infiltrations showed beginning neuronophagia, satellitosis and other slight disintegrative changes (fig. 2 *B*).

Diencephalon and mesencephalon: There was nothing of note in the myelin sheath preparations. In the cresyl violet preparations a few vessels in the thalamus, hypothalamus, internal capsule, substantia nigra and mesencephalon showed the same perivascular reaction as was noted in the cortex. These infiltrations consisted of a mixture of inflammatory cells and compound granular corpuscles. The

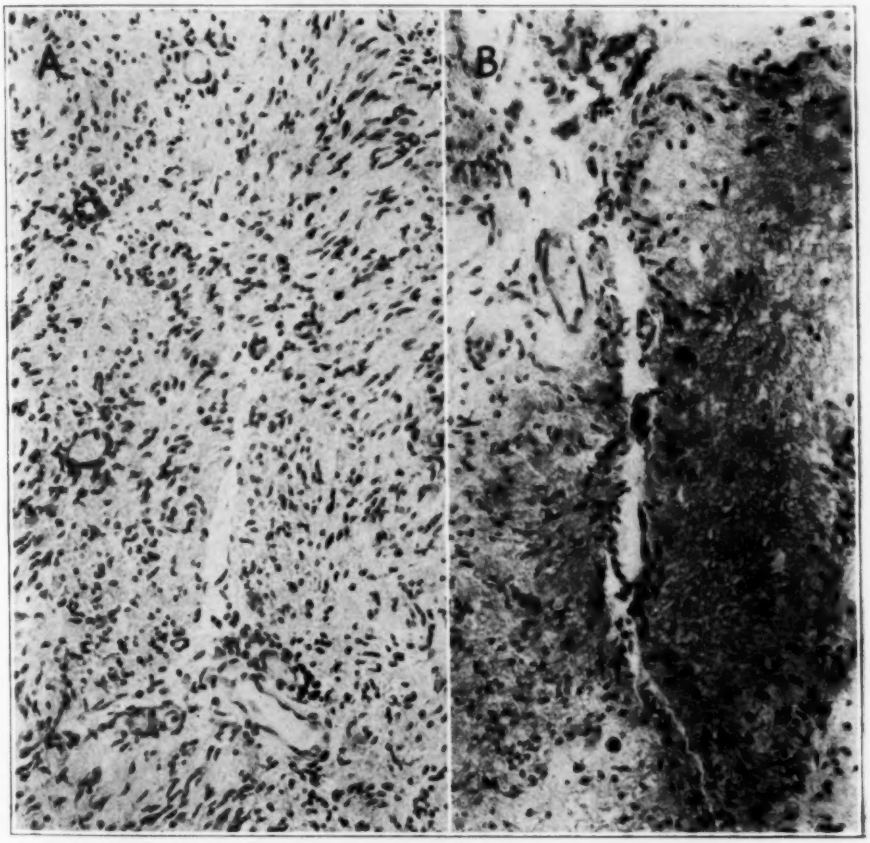

Fig. 5 (case 1).—*A*, perivascular infiltration and slight proliferation of vessels in the roots. *B*, necrosis of roots. Cresyl violet; × 100.

perivascular infiltrations were more numerous in the cerebral peduncles. There was also an increase in microglia cells. Areas of demyelination, however, were not present.

Optic nerves and tracts: These structures, especially the tracts, disclosed perivascular demyelination with slight swelling of the myelin sheaths (fig. 3). Occasional perivascular infiltrations with lymphocytes and compound granular cells were observed in these regions. Holzer preparations revealed slight perivascular gliosis and astrocytic proliferation.

Pons: Sections of the pons through the nuclei of the third and fourth nerves disclosed the same slight perivascular infiltration as that seen in other regions. The ganglion cells near these areas disclosed neuronophagia and chromatolysis; this was best observed in nerve cells of the nuclei of the third and fourth nerves.

Medulla oblongata: The vessels of the pyramids and a few vessels on the upper pole of the olives showed a perivascular reaction similar to that seen in other parts of the central nervous system. Some of the nerve cells of the nuclei of the ninth and tenth nerves stained poorly and showed neuronophagia. There

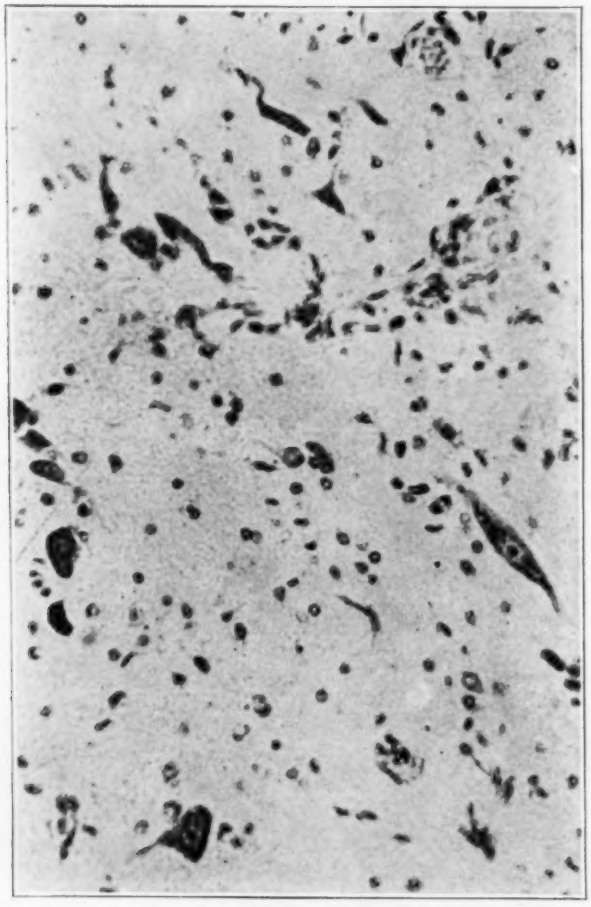

Fig. 6 (case 1).—Diminution in number and shrinkage of anterior horn cells. Cresyl violet; × 200.

was a slight increase in the microglia cells in the region of the dorsal nucleus of the tenth nerve.

Cerebellum and dentate nucleus: A few vessels showed perivascular infiltrations. The Purkinje cells and the nerve cells of the dentate nuclei were well preserved.

Spinal cord: In the myelin sheath preparations the ventrolateral tracts, especially in the lower thoracic region, stained poorly as compared with the posterior tracts, but no changes could be demonstrated with any of the delicate

stains, such as the Marchi stain and sudan III. The roots, including their zones of entrance, were severely demyelinated throughout all regions. This was most pronounced in the sacral area (fig. 4). With the high power lens, hardly any myelin could be seen in these roots. The vessels of the roots were congested. There was also occasional proliferation of vessels, with deposits of iron pigment and lymphocytes (fig. 5 *A*). The architectural arrangement of some of the roots was completely distorted, and other roots showed actual necrosis (fig. 5 *B*). In the cresyl violet preparations the cervical region showed nothing of note.

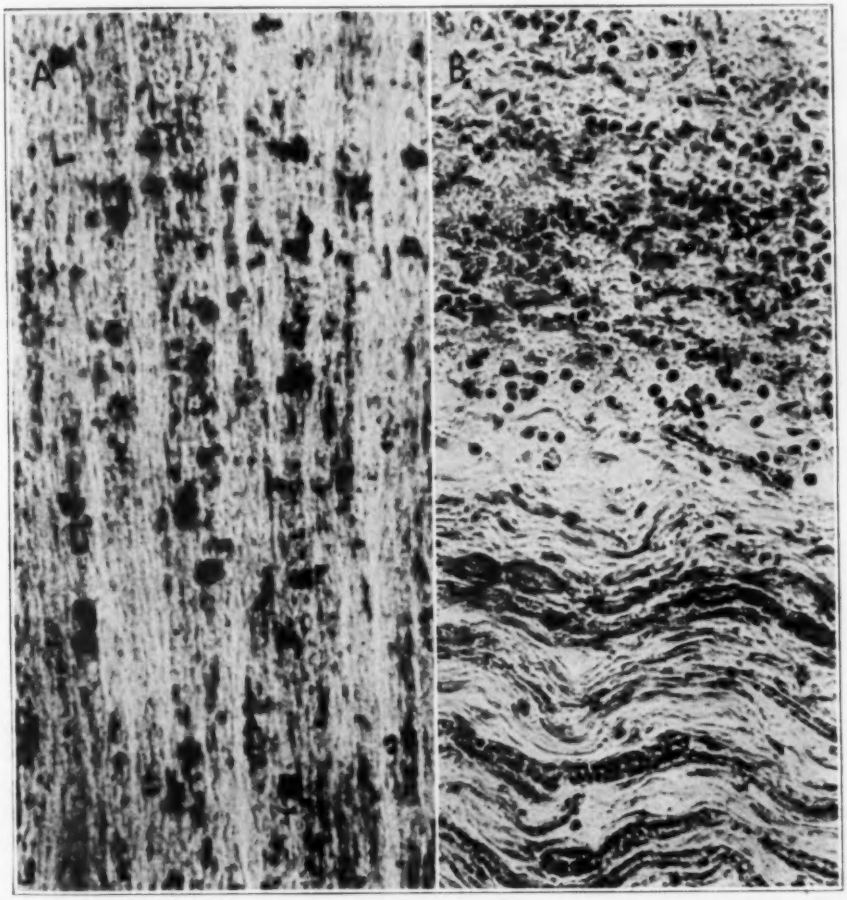

Fig. 7 (case 1).—*A*, breaking down of myelin, with deposition of fat; Marchi stain, × 70. *B*, disintegration of myelin and inflammatory process within a peripheral nerve; sudan III, × 200.

In the upper thoracic region there were edema of the pia-arachnoid and an inflammatory process of the meninges, consisting of lymphocytes, plasma and endothelial cells. An occasional nerve cell was shrunken. In the lower thoracic region there were notable diminution in number and shrinkage of nerve cells and increase in glia cells (fig. 6). The nerve cells of the sacral region also showed vacuolation.

Peripheral nerves: In the Marchi preparations there was disintegration of the myelin, with a few fatty globules, throughout all the nerves, most intense

in the brachial plexus and in the lumbosacral region (fig. 7 *A*). In the sudan III preparations, although there were no large deposits of fat in the conspicuously degenerated areas, the swollen nerve fibers and the fibers which were partly preserved disclosed fine lipid deposits, which stained paler than ordinary fat. Fat globules were also noted occasionally. The vessels of the nerves showed a collection of inflammatory cells, consisting of lymphocytes, plasma cells and endothelial cells (fig. 7 *B*). There were no iron deposits in these perivascular spaces. Some of the lymphocytes had actually penetrated the adventitia. The perineural

Fig. 8 (case 1).—*A*, destruction of myelin in peripheral nerves; Spielmeyer method, × 200. *B*, extreme swelling and disintegration of the axis-cylinders, with bulbous process; Bielschowsky stain, × 400.

spaces were loaded with lipid deposits. In myelin sheath preparations some of the myelin sheaths in various nerves, especially the sciatic, had completely disappeared; others were slightly swollen and fragmented (fig. 8 *A*). Still others were broken up and greatly swollen. There was hardly a normal fiber. In the Bielschowsky preparations the axis-cylinders disclosed disintegration, bulbous swellings and corkscrew processes (fig. 8 *B*). Swelling was the most prominent feature. In places inflammatory cells were seen.

Comment.—The lesions in this case were scattered throughout the entire nervous system, involving the cortex, mesencephalon, metencephalon, spinal cord, nerve roots and peripheral nerves. The pathologic process was severest in the roots and the peripheral nerves. The process was characterized by a mild inflammatory reaction throughout. The absence of early evidence of sensory disturbances may be due to the possibility that degeneration of the posterior roots took place late in the course of the illness.

The clinical picture in this case resembled that originally described by Guillain, Barré and Strohl except for the fatal termination. The laboratory findings were also similar.

CASE 2.[6]—J. K., a man aged 63, became ill about June 15, 1940. A dull pain appeared in the right shoulder; it soon spread and involved the right arm and then the left arm; within one week pain involved both lower limbs. The pain in the limbs was severe enough to awaken him at night. Numbness and weakness quickly beset the four limbs, especially the lower ones; the weakness forced him to take to bed. There was no paresthesia or muscular twitching and no defect in sphincter control. He was admitted to the Hospital for Joint Diseases on July 1, under the care of Dr. Martin Vorhaus. There was a past history of gonorrhea, syphilis, malaria and yellow fever in early adult life. At the age of 50 a cyst was removed from the thyroid.

On July 10 the patient was seen by one of us (S. B.). He presented the clinical picture of polyneuritis. The muscles of all the limbs were weak; all the deep reflexes were absent, as were the abdominal and cremasteric reflexes. Pressure on the calves elicited pain. All forms of sensation were diminished from the knees and elbows down. Facial weakness was present bilaterally, being more pronounced on the left side. There was hoarseness of recent onset, due presumably to weakness of the laryngeal muscles. (On July 2, indirect laryngoscopic examination did not reveal any visible lesion of the larynx or immobility of the vocal cords, but the examination was unsatisfactory because of gagging.) The cranial nerves were otherwise normal. Breathing was mainly abdominal. His blood pressure was 100 systolic and 60 diastolic.

During July 1940 some improvement appeared in the motor power of the upper limbs and weakness of the left side of the face decreased. About August 7 episodic mental confusion, with loss of memory, was noted. Orientation was retained. On August 18 the patient became irrational, agitated and disoriented. Mental confusion continued, being less at times. On August 30 he was disoriented and confused and kept repeating senseless phrases. Speech was unclear, hoarse and nasal, but the palate arched well. Facial paralysis was still evident, especially on the left. There was considerable wasting of all muscles of the limbs, and all the deep reflexes were absent. Breathing was mainly abdominal. Within the next few days, dyspnea, cyanosis and increased perspiration of the face and neck appeared. The patient became drowsy and finally comatose. On September 3 there was pitting edema of the left leg and a maculopapular rash appeared on the thigh. Bronchopneumonia and phlebitis of the left leg set in, associated with elevation of temperature to 103 F. A restless thrashing about, irrational behavior and screaming were clinical features. The temperature, pulse and respirations had been normal until August 29, when the temperature rose, ranging from 100.2 to 104 F. until

6. Dr. Martin Vorhaus gave us permission to report this case.

death; there was a preterminal rise to 106 F.; the Cheyne-Stokes type of breathing also preceded death.

Laboratory Data.—Several urinalyses revealed nothing significant. Three blood counts were reported as follows:

July 2: Hemoglobin, 13.5 Gm. per hundred cubic centimeters; red cells, 4,480,000, and white cells, 8,400, with 65 per cent segmented neutrophils, 4 per cent nonsegmented neutrophils, 3 per cent eosinophils, 1 per cent basophils, 26 per cent lymphocytes and 1 per cent monocytes.

August 28: Hemoglobin, 12 Gm. per hundred cubic centimeters; red cells, 4,000,000, and white cells, 7,800, with 70 per cent segmented neutrophils, 2 per cent eosinophils and 28 per cent lymphocytes.

September 11: Hemoglobin, 10.5 Gm. per hundred cubic centimeters; red cells, 3,680,000, and white cells, 11,700, with 78 per cent segmented neutrophils, 2 per cent nonsegmented neutrophils, 2 per cent eosinophils, 12 per cent lymphocytes and 3 per cent monocytes.

The sedimentation rate (July 11) was 12 mm. in one hour. On July 2 the Kahn and Kline reactions of the blood were negative.

Examination of the spinal fluid (July 2) revealed a clear fluid, under a pressure of 140 mm. of water. There was no evidence of block. The fluid showed a trace of globulin, 77 mg. of sugar per hundred cubic centimeters, negative reactions to the Kahn and Kline tests and a colloidal gold curve of 111100000. Unfortunately, no estimation of the protein content was made. Specimens of urine were sent to Dr. A. Gettler's laboratory for examination for the presence of heavy metals (lead and arsenic); none was found.

Autopsy.—General Observations: The diagnosis was bronchopneumonia, lower lobe of the right lung; organizing embolus in the right pulmonary artery; pulmonary congestion and edema; chronic pulmonary emphysema; coronary sclerosis; diverticulosis of the colon, and adenomatous polyps of the sigmoid.

Gross examination of Brain and Spinal Cord: No gross abnormalities were noted.

Microscopic Examination: Blocks from various cortical regions, the basal ganglia, the pons, the medulla oblongata and the spinal cord were embedded. Sections were cut and stained by the myelin sheath and cresyl violet methods. The peripheral nerves were stained by the Marchi, Weigert, Bodian and hematoxylin-eosin methods.

Cortex: No abnormalities were noted in the myelin sheath preparations. In the cresyl violet preparations the meninges showed slight thickening due chiefly to the presence of proliferating arachnoidal cells. The meningeal vessels showed moderate atherosclerotic changes. The cytoarchitectural layers of the cortex had a normal arrangement. An occasional engorged vessel was noted.

Diencephalon and basal ganglia: A few distended vessels were noted in the thalamic nuclei and in the putamen. No areas of demyelination were noted. In cresyl violet preparations the nerve cells of the putamen and the pallidum were normal. The perivascular spaces were somewhat distended. The nerve cells of the thalamus and hypothalamus were normal. There was pigment atrophy of some of the nerve cells of the hypothalamus. In sections through the pulvinar a few lacunas were noted. In the cresyl violet preparations numerous colon bacilli were noted in some of the vessels. A few vessels in this region were filled with lymphocytes.

Pons: Sections through the aqueduct of Sylvius showed no abnormalities in the myelin sheath preparations. In the cresyl violet preparations, there was some

pigment atrophy of the nerve cells of the nuclei of the ocular nerves and in some of the pontile nerve cells.

Medulla oblongata: No abnormalities were noted in the myelin sheath preparations. The cresyl violet preparations revealed a few amyloid bodies in the pyramids.

Cerebellum: Sections of this region disclosed slight swelling of the Purkinje cells.

Spinal cord: The myelin sheath preparations showed a slight pallor of the anterior roots at practically all levels. In the thoracic region there was also pallor

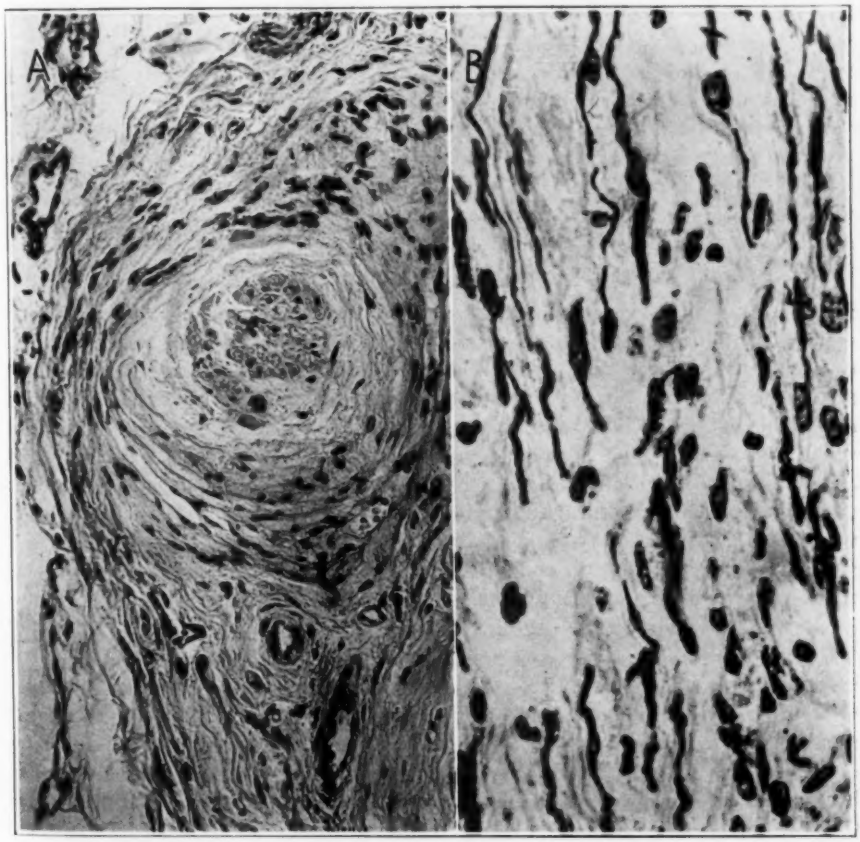

Fig. 9 (case 2).—*A*, onion-peel arrangement in a peripheral nerve; hematoxylin-eosin stain, × 150. *B*, swelling and slight disintegration of axis-cylinders; Bodian method, × 400.

of some of the posterior roots. Actual destruction of myelin sheaths could not be seen. In the gray matter of the midthoracic region there was dilatation of the perivascular spaces. Creysl violet preparations showed distention of the meninges without inflammatory reaction. The anterior horn cells were normal except for a few, which showed pigment atrophy. Some of the vessels of the gray matter were engorged. In some regions of the cord there were numerous amyloid bodies. In the lower thoracic region, one of the roots contained numerous psammoma bodies and two of the vessels in the posterior part of the cord showed atherosclerotic

changes, while two others showed hyaline degeneration. No actual pathologic change was noted in the cord at this level. In the lumbosacral region no abnormalities were noted except for pigment atrophy in the anterior horn cells. An occasional chromatolytic nerve cell was observed.

Peripheral nerves: The left brachial plexus showed destruction of the myelin sheaths. With the hematoxylin-eosin method, some of the nerve fibers in the right brachial plexus had an onion-peel arrangement (fig. 9 *A*), suggestive of that seen in progressive hypertrophic interstitial neuropathy (Dejerine-Sottas neuropathy). The demyelination was severe in the left posterior tibial nerves. With the Marchi stain, there was swelling of the Schwann nuclei. The blood vessels showed moderate atherosclerosis but no inflammatory changes. In places there was thickening of the perineural sheaths. The Bodian stain revealed breaking down, swelling and a corkscrew appearance of the axis-cylinders (fig. 9 *B*). The axis-cylinders were not so severely destroyed as the myelin sheaths. There was pronounced swelling of the Schwann nuclei at the periphery. Extensive changes were also observed in the right lumbosacral plexus. In the hematoxylin-eosin preparations there was swelling of the Schwann nuclei. The vessels showed moderate sclerotic changes. No inflammatory changes were noted. The perineural sheaths were thickened.

Case 3.—D. G., a man aged 34, was admitted to the Montefiore Hospital on June 5, 1939, with a history of generalized weakness, inability to walk and loss of weight. His illness began in February 1938, though he had been easily fatigued for three years prior to this time. Weakness first appeared in the muscles of the calves; a month later his gait became awkward. In May 1938 he felt a burning pain in the soles, and in July of that year the skin of both legs below the knees became "purplish." The symptoms gradually grew worse. He was frequently awakened by severe pain. During this time he lost 25 pounds (11.3 Kg.) in weight, and a heavy pigmentation of the skin appeared "like a sunburn." In September 1938 he had an attack of angioneurotic edema, associated with a brief episode of bloody diarrhea, the cause of which could not be ascertained. There was no history of exposure to heavy metals or other injurious substances. The family history was not contributory.

He was admitted to the Neurological Institute of New York on Oct. 11, 1938 and discharged on Jan. 24, 1939. At that time examination disclosed weakness and atrophy of most of the muscles of the upper extremities, especially the pectoral, deltoid and triceps muscles; a mild defect in all types of sensation, with a fairly definite level at the junction of the thoracic and the lumbar dermatomes; loss of vibratory sensibility below the third lumbar vertebra, and hyperesthesia of the soles. When he was on his feet, there was cyanosis of the extremities. All the deep reflexes were absent except for a slight response of the biceps. Loss of muscular power was about 20 per cent in the lower extremities and 75 per cent in the upper extremities. His mental status was normal except for slight depression of mood.

Laboratory Data.—At the Neurological Institute of New York, the Wassermann reactions of the blood and the spinal fluid were negative. The spinal fluid was under normal pressure, with 110 mg. of total protein per hundred cubic centimeters; a reaction for globulin of 2 plus; 53 mg. of sugar and 670 mg. of chlorides, per hundred cubic centimeters, and a colloidal gold curve of 1111222321. Gastric analysis revealed a normal condition. Chemical analysis of the blood revealed 12.3 mg. of urea nitrogen, 84 mg. of sugar and 0.1 mg. of ascorbic acid, per hundred cubic centimeters. A five hour specimen of urine showed dextrose tolerance of 5 per

cent. The blood count was as follows: hemoglobin, 106 per cent; red cells, 5,660,000; color index, 0.9, and white cells, 10,650, with 67 per cent polymorphonuclear cells, 30 per cent lymphocytes, 2 per cent monocytes and 1 per cent basophils. The sedimentation rate was 15 mm. in one hour. The serum chloride measured 570 mg. and the blood cholesterol 133 mg., per hundred cubic centimeters; the serum sodium, 138 mg. per liter; the blood calcium, 9.5 mg., and the blood phosphorus, 4.1 mg., per hundred cubic centimeters; the dextrose tolerance curve was normal. The fasting blood sugar was 78 mg. per hundred cubic centimeters. The serum protein was 6.9 Gm.; serum albumin, 4.3 Gm.; serum globulin, 2.6 Gm., and serum euglobulin, 0.4 Gm., per hundred cubic centimeters. The urine was normal except for 5 white cells per high power field. Analysis of the urine for lead gave negative results. On Oct. 10, 1938, the spinal fluid showed 7 cells per cubic millimeter, 168 mg. of total protein per hundred cubic centimeters, a 2 plus reaction for globulin and 64 mg. of sugar per hundred cubic centimeters. On November 3 the protein was 222 mg.; the reaction for globulin, 2 plus, and the sugar, 68 mg. per hundred cubic centimeters. Repeated examinations of the spinal fluid disclosed a similar picture. Examination of the stools showed nothing abnormal. Roentgenograms of the skull, vertebrae, chest and gastrointestinal tract showed a normal condition except that the shadow of the liver extended down somewhat farther than usual and the roentgenograms of the skull and the lumbar portion of the spine disclosed multiple areas of increased density, indicating the possibility of early Paget's disease (osteitis deformans). Peripheral vascular examination disclosed generalized dilatation of capillaries, due to disturbance in the vasconstrictor mechanism, with resulting congestion of blood in venous capillaries and subcapillary plexuses.

At one time, a coarse nystagmus, more prominent on the right side, and a tendency to dorsiflexion of the left great toe were noted. Three times during the patient's stay at the hospital, angioneurotic edema of the face and tongue developed. This condition cleared up rapidly after epinephrine was administered. He was given high vitamin diet and large amounts of thiamine hydrochloride. He was transferred to Bellevue Hospital with the diagnosis of encephalomyeloradiculitis—Guillain-Barré type.

At Bellevue Hospital, examination disclosed the same clinical picture. Cutaneous temperatures indicated sympathetic paralysis of the lower extremities and partial dysfunction in the upper ones. The liver and spleen were palpable. The optic disks showed nasal blurring and congestion. Repeated examinations of the spinal fluid showed the protein-cellular dissociation, with total protein levels up to 200 mg. per hundred cubic centimeters. During the last two months of his stay at Bellevue Hospital, the patient showed considerable improvement in muscular power, so that he was able to take a few steps. Reactions to tests for allergy were negative for everything but ragweed. He was discharged to Montefiore Hospital on June 5, 1939.

At Montefiore Hospital, examination disclosed uniform gray-brown discoloration of the skin, with no pigmentation of the mucous membranes. The blood pressure was 126 systolic and 80 diastolic. The liver and spleen were palpable. Slight generalized lymphadenopathy was present. The extremities had a cyanotic hue, and the temperature was the same as that of the environment. There was moderate pitting edema of both lower extremities.

Neurologic examination disclosed generalized muscular atrophy, more advanced about the shoulder girdle and in the interosseous muscles of both hands; bilateral foot and hand drop, and contractures of the hands and feet. All the deep reflexes

and the abdominal and cremasteric reflexes were absent. The ulnar and common peroneal nerves were tender but not enlarged. There was pronounced diminution of all sensations in the upper and lower extremities, of the glove and stocking variety. Pseudoathetoid movements were present in the fingers, and a Chovstek sign was elicited. There were areas of "hyperpathia," especially about the right anterior cubital fossa and on both soles. Two point discrimination was slightly impaired in the hands.

The edema of the lower extremities was regarded as possibly due to renal disturbance or to changes in the lateral horn cells; pigmentary disturbances were attributed to endocrine imbalance, perhaps disease of the adrenal glands.

Laboratory Data.—Chemical analysis of the blood, including determinations of the calcium and phosphorus, gave normal values. Urinalysis, including tests for heavy metals and polyporphyrins, revealed nothing significant. Biopsy of the skin, like gastric analysis, revealed nothing unusual. A roentgenogram of the skull showed islands of increased density of bone. Repeated spinal punctures disclosed 6 to 8 cells per high power field, with protein as high as 222 mg. per hundred cubic centimeters.

Biopsy of the anterior tibial muscle showed mild atrophy.

Electroencephalographic tracings revealed no abnormal changes.

The patient was treated with various preparations of vitamins and hormones, to no avail. In January 1941 ascites appeared and abdominal punctures were done frequently. Examination of the ascitic fluid revealed nothing significant.

The liver and spleen continued to shrink, and just prior to death they were not palpable. The patient died on Feb. 12, 1942.

Autopsy.—General Observations: The diagnosis was hepatomegaly, splenomegaly, generalized lymphadenopathy, reticuloendotheliosis and generalized lymphocytic infiltration of various tissues.

The hyperplasia of the reticuloendothelial system in the absence of the universal round cell infiltration suggested to the pathologist a general low grade chronic infection, probably of virus origin. There seemed to be no relation between the hepatomegaly and splenomegaly and the peripheral neuropathy.

Gross Examination of the Nervous System: Brain: The pia-arachnoid had a glistening appearance. It was adherent to the convolutions but could be stripped readily. The pacchionian granulations were prominent. The vessels of the cerebral hemispheres were congested. The cranial nerves and the vessels at the base were normal. The white matter had an anemic appearance. No other gross abnormalities were noted.

Spinal cord: The spinal cord showed no gross abnormalities except for thinning. There was some translucency of the posterior columns.

Microscopic Examination of the Nervous System: Sections of the cortex, diencephalon, basal ganglia, mesencephalon, pons, cerebellum, medulla oblongata and spinal cord were stained by the myelin sheath and cresyl violet methods. Sections of the spinal cord and peripheral nerves were stained by the Marchi, Spielmeyer, sudan III and cresyl violet methods.

Cortex: In the myelin sheath preparations there was slight pallor of the white matter but no destruction of myelin sheaths. In the cresyl violet preparations the meninges were normal. The architectural arrangement of the cortex was normal. A few nerve cells showed water cell changes; no other abnormality was noted. In the white matter of the cortex there was occasional swelling of the oligodendroglia cells.

Diencephalon and basal ganglia: The myelin sheath preparations revealed slight pallor of the globus pallidus. With high power magnification, occasional

swollen myelin sheaths were noted in the pallidum. The striatum had a normal appearance. The large and small nerve cells stained normally. There were some calcified vessels and calcific deposits in the pallidum, surrounded by slight areas of devastation. There seemed to be disappearance of some nerve cells and a shadow-like appearance of others. The nerve cells of the hypothalamus were normal. The nerve cells of the substantia nigra did not contain the usual amount of pigment.

Midbrain and Medulla: Myelin sheath and cresyl violet preparations through the aqueduct of Sylvius showed no abnormality. Sections through the fourth ventricle

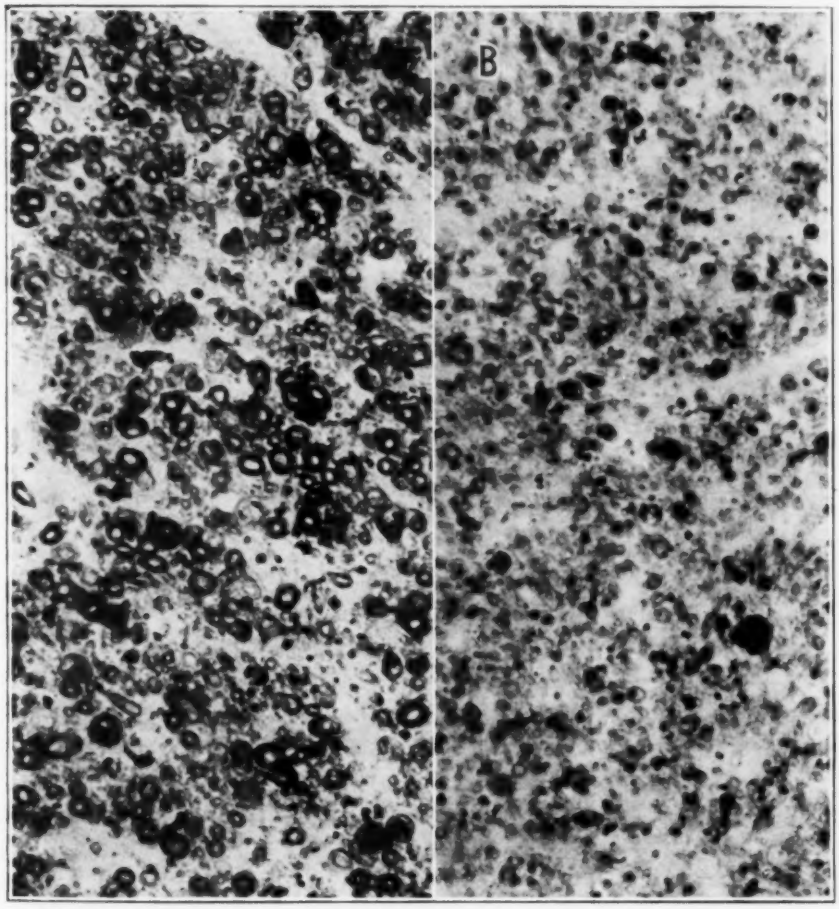

Fig. 10.—*A*, normal myelin sheaths in the posterior columns of the spinal cord. *B* (case 3), fatty globules in the posterior columns, to be compared with *A*; Marchi stain, × 200.

revealed a normal condition. There was an occasional glial rosette in the region bordering the fourth ventricle. No other changes were observed in the medulla oblongata. In some sections of the cerebellum there was occasional perivascular infiltration, consisting of a few lymphocytes, plasma cells and endothelial cells. An occasional ischemic nerve cell was noted in the dentate nucleus. The Purkinje cells were within normal limits.

Spinal cord: No abnormalities were noted in the myelin sheath preparations except for an occasional swollen myelin sheath in the posterior columns of the lower thoracic region. In the sudan III preparations the same process was noted, but fat could not be demonstrated within the cord. The posterior roots showed occasional destruction and swelling of myelin. The anterior roots stained better than the posterior roots. In the Marchi preparations the dorsal columns of the lumbar portion of the cord showed breaking down of myelin and heavy black pigment granules (fig. 10 *B*). Some of the posterior and anterior roots also contained a few black granules. In the cresyl violet preparations there were amyloid bodies, especially in the posterior columns, and a slight increase in proliferating astrocytes. The meninges of the cord were distended but otherwise normal. In the gray matter there were numerous agonal hemorrhages, with slight breaking down of red blood cells in a few areas. The anterior horn cells amid these hemorrhages were well preserved. Here and there, an occasional chromatolytic nerve cell was noted.

Peripheral nerves: The Spielmeyer preparation showed severe destruction of some of the myelin sheaths and beading of others. The axis-cylinders showed swelling, disintegration and bulbous terminations. The architectural arrangement of almost every fiber was distorted. About half or more of the fibers had disappeared. In the Marchi preparations the same process was noted; with this stain numerous deposits of black granules could be demonstrated. The cresyl violet preparations showed elongation and proliferation of the nuclei of Schwann. There was also slight proliferation of the vessels.

COMMENT

Viets[7] and Cobb and Coggeshall[8] pointed out that cytoalbuminous dissociation may be found with other neuritides. In their analysis of the cerebrospinal fluid of 30 patients with infectious polyneuritis, Merritt and Fremont-Smith[9] found a normal protein content in only 8 though the cell count was normal in 80 per cent. The presence of cytoalbuminous dissociation was definitely proved in 2 of our 3 cases. It varied from 94 to 240 mg. in case 1 and from 125 to 222 mg. per hundred cubic centimeters, in case 3. The protein content of the cerebrospinal fluid tends to increase in the acute phase of the disease, and this, according to our experience, may be observed not only with polyneuritis but also with many other diseases of the spinal cord. Indeed, the question may be raised whether the presence of cytoalbuminous dissociation has any particular etiologic importance.

Regarding the extent of the pathologic process beyond the peripheral nerves, Bradford, Bashford and Wilson demonstrated changes in the posterior roots, involvement of the nerve cells of the spinal cord with

7. Viets, H. R.: Acute Polyneuritis with Facial Diplegia, Arch. Neurol. & Psychiat. **17**:794 (June) 1927.

8. Cobb, S., and Coggeshall, H. S.: Neuritis, J. A. M. A. **103**:1608 (Nov. 24) 1934.

9. Merritt, H. H., and Fremont-Smith, F. F.: The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Company, 1938.

perineural lymphocytic infiltration and a similar process about the nerve cells of the deeper layers of the cortex with very little neuronal change. Viets described changes in the nuclei of the seventh nerve and slight changes in the anterior horn cells of the spinal cord. Gilpin, Moersch and Kernohan [10] mentioned changes in the posterior root ganglia and pontile nuclei in 1 of their cases. In their 3 fatal cases, Roseman and Aring [11] described the main pathologic process in the peripheral nerves. They also observed abnormalities in the spinal roots and ganglia, the cauda equina and the cells of the gray columns of the spinal cord (especially in the cervical and thoracic regions, with the greatest involvement of cells in the ventral gray columns) and some changes in the myelin sheaths and axis-cylinders in the pathways of the spinal cord. Involvement of the brain stem, especially the nerve cells of the olivary nuclei, the tractus solitarius, the nucleus ambiguus, the dorsal motor nucleus of the vagus nerve and the facial nuclei, and minor changes in the other cranial nerve nuclei were also described. Slight changes were also seen in various parts of the cortex and cerebellum. Roseman and Aring expressed the opinion that the changes in the central nervous system were of a readily reversible nature.

In our 3 cases widespread pathologic changes were observed, especially in case 1: The severest changes were seen in the peripheral nerves, those of next greatest intensity in the roots and spinal cord and those of least severity in the diencephalon and cortex. The optic nerves and tracts were involved in this case, accounting for the correlated clinical findings. In case 2, the spinal cord and higher neural structures were not involved. Interestingly, the changes in the peripheral nerves resembled slightly those seen in the Dejerine-Sottas type of hypertrophic neuropathy. The patient gave a history of early syphilis, but the serologic reactions were negative and clinical evidence of syphilitic involvement of the central nervous system was absent. In case 3, in addition to involvement of the peripheral nerves, there were changes in the spinal roots and posterior columns, slight perivascular infiltration in the cerebellum and glial rosette formation in the medulla oblongata.

115 East Sixty-First Street.

1155 Park Avenue.

10. Gilpin, S. F.; Moersch, F. P., and Kernohan, J. W.: Polyneuritis: A Clinical and Pathologic Study of a Special Group of Cases Frequently Referred to as Instances of Neuronitis, Arch. Neurol. & Psychiat. **36**:937 (May) 1936.

11. Roseman, E., and Aring, C. D.: Infectious Polyneuritis, Medicine **20**:463, 1941.

RELATION OF THE FRONTAL LOBE TO THE AUTONOMIC NERVOUS SYSTEM IN MAN

MAX RINKEL, M.D.

MILTON GREENBLATT, M.D.

GAYLORD P. COON, M.D.
AND
HARRY C. SOLOMON, M.D.
BOSTON

BILATERAL subcortical section of the frontal lobe of the brain was introduced to this country by Walter Freeman and James Watts [1] in 1936 for the treatment of serious mental conditions. In the course of the many hundreds of operations which have been performed, clinical observations have indicated a close relation of the frontal lobes to the autonomic nervous system. Sudden fall in blood pressure, relief from indigestion and palpitation, decrease in the blood sugar level, changes in gastrointestinal functions, sudden outbursts of rage, trembling, perspiration and occasional angioneurotic edema are some of the clinical observations after lobotomy which relate to the autonomic nervous system. Neurophysiologic investigations on animals in the past few years have uncovered fundamental facts with regard to cortical representations of the autonomic nervous system. Inhibition of respiration, rise of blood pressure and decrease in the tonus of the gastric musculature on electrical stimulation of the orbital surface of the frontal lobes in both cats and monkeys were reported by Bailey and Sweet.[2] Complex autonomic responses to excitation of the rostral part of the

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From the Department of Psychiatry, Harvard Medical School, and the Boston Psychopathic Hospital, Dr. Harry C. Solomon, Director.

Able technical assistance was given by Miss Marie M. Healey and Mrs. Helen Mott, of the electroencephalographic laboratory, Boston Psychopathic Hospital.

1. Freeman, W., and Watts, J. W.: Psychosurgery, Springfield, Ill., Charles C Thomas, Publisher, 1942.

2. Bailey, P., and Sweet, W. H.: Effects on Respiration, Blood Pressure and Gastric Motility of Stimulation of Orbital Surface of Frontal Lobe, J. Neurophysiol. **3**:276-281 (May) 1940.

cingulate gyrus, Brodman's area 24, were obtained by Smith [3] in the monkey Macaca mulatta. Kennard,[4] by means of the ablation technic, investigated corticoautonomic representations in cats and monkeys. In the cat, bilateral removal of the frontal lobe is followed by all the symptoms of sham rage. In the monkey, similar signs of release of autonomic function follow the same procedure, but no sham rage results. The subcortical bilateral prethalamic section of the frontal lobe for psychosurgical reasons presented an opportunity to investigate in man the relation of the frontal lobes to the autonomic nervous system.

METHOD OF INVESTIGATION

A total of 95 patients were examined, of whom 29 had undergone prefrontal lobotomy. The control group consisted of 14 volunteer medical students and nurses and 52 hospital patients. A number of the latter had received various forms of shock treatment.

The autonomic nervous system was tested (1) pharmacologically and (2) by stimulation of the carotid sinus. The pharmacologic test was restricted to the intravenous injection of 0.05 mg. of epinephrine hydrochloride (1:1,000), which ordinarily causes only a slight change in blood pressure and pulse rate, and little or no untoward reaction. The effects of cholinergic drugs are not reported because of the difficulty encountered in preliminary experiments in evaluating their comparative effects. Reitman [5] evidently had the same difficulty, judging by the inconclusive results that he reported in a preliminary paper. We, therefore, have used the carotid sinus reflex as a method to test the functions of the parasympathetic system. The result of stimulation of the carotid sinus is unequivocal, and positive reflexes are rare among normal persons. Furthermore, since neither the immediate afferent or efferent pathway of the carotid sinus reflex arc is affected by lobotomy, it could be assumed that a pronounced increase in the incidence of the positive carotid sinus reflex in lobotomized patients would provide information concerning the functions of the frontal lobes. The effect of unilateral and of bilateral stimulation of the carotid sinus was observed clinically and by means of simultaneous electrocardiographic and electroencephalographic tracings.

RESULTS

The Sympathetic Nervous System.—This system responded to the intravenous injection of 0.05 mg. of epinephrine hydrochloride (1:1,000) differently in patients on whom lobotomy had been performed and in hospital patients who had not undergone this operation. Also, there was a striking difference in the reactions of the same patient when he was tested before and after the operation. Table 1 shows the effect of

3. Smith, W. K.: The Functional Significance of the Rostral Cingular Cortex as Revealed by Its Responses to Electrical Excitation, J. Neurophysiol. **8**:241-255 (July) 1945.

4. Kennard, M. A.: Focal Autonomic Representation in the Cortex and Its Relation to Sham Rage, J. Neuropath. & Exper. Neurol. **4**:295-304 (July) 1945.

5. Reitman, F.: Autonomic Responses in Prefrontal Leucotomy, J. Ment. Sc. **91**:318-321 (July) 1945.

intravenous injection of 0.05 mg. of epinephrine hydrochloride on the systolic blood pressure, the height of which was reached within one minute. The average increase in the systolic blood pressure in patients with lobotomy was 85.1 mm. of mercury, as compared with 42.4 mm. in patients of the hospital who had not been operated on. Table 1 also shows that patients were tested from four to one hundred and twenty days after the operation but that the time interval had no effect on the response. There was a slight difference in the reactions of patients who had received electric or insulin shock treatment; however, the number

TABLE 1.—*Rise in Systolic Blood Pressure of Patients With and Without Lobotomy on Intravenous Injection of 0.05 mg. of Epinephrine Hydrochloride*

Hospital Patients					
			After EST : IST *		
Record No.	Mm. Hg	Time of Reaction, Min.	Record No.	Mm. Hg	Time of Reaction, Min.
7	50	1	2	30	1
	50	1	3	20	1
	60	1	4	50	1
	40	1	5	60	1
	40	1	6	20	2
	50	1	9	30	1
	45	1	18	50	1
17	40	1	19	30	1
27	50	1	69	50	1
	Average: 47.2 mm.			Average: 37.7 mm.	
	Total average: 42.0 mm. Hg				

Patients After Lobotomy							
Record No.	Mm. Hg	Time of Reaction, Min.	Days After Operation	Record No.	Mm. Hg	Time of Reaction, Min.	Days After Operation
1	60	1	13	20	120	1	26
	70	1	68	22	70	1	26
4	80	1	4	21	90	1	26
	110	1	8	26	100	1	27
	92	1	24	43	70	1	16
9	70	1	13	44	80	1	8
11	100	1	20	54	80	1	17
18	90	2	25	59	80	1	5
	Total average: 85.1 mm. Hg						

* EST and IST indicate previous electric and insulin shock treatments.

of patients tested was too small to allow any conclusive deductions. Table 2 demonstrates the difference between the rise of the pulse pressure in the lobotomized patients, with an average of 60.8 mm. of mercury, and that in the control group, with an average of 26.3 mm. Pilomotor reactions and shivering were more frequently observed in patients on whom lobotomy had been performed.

The notable difference in the response to epinephrine hydrochloride (0.05 mg., given intravenously) is accentuated by a comparison of the effects in the same patient before and after lobotomy (fig. 1).

On the basis of these observations, the question arises whether the greater reaction of the sympathetic nervous system after lobotomy

is due to an elimination of vagal inhibition. In favor of this theory are the following facts: 1. Similarity in rise of the systolic blood pressure induced with epinephrine in patients after lobotomy and in normal persons after inhibition of the vagus nerve with atropine (fig. 2). 2. Relation of the orbital surface of the frontal pole to vagal function. Kennard [6] reported that bilateral removal of this region in

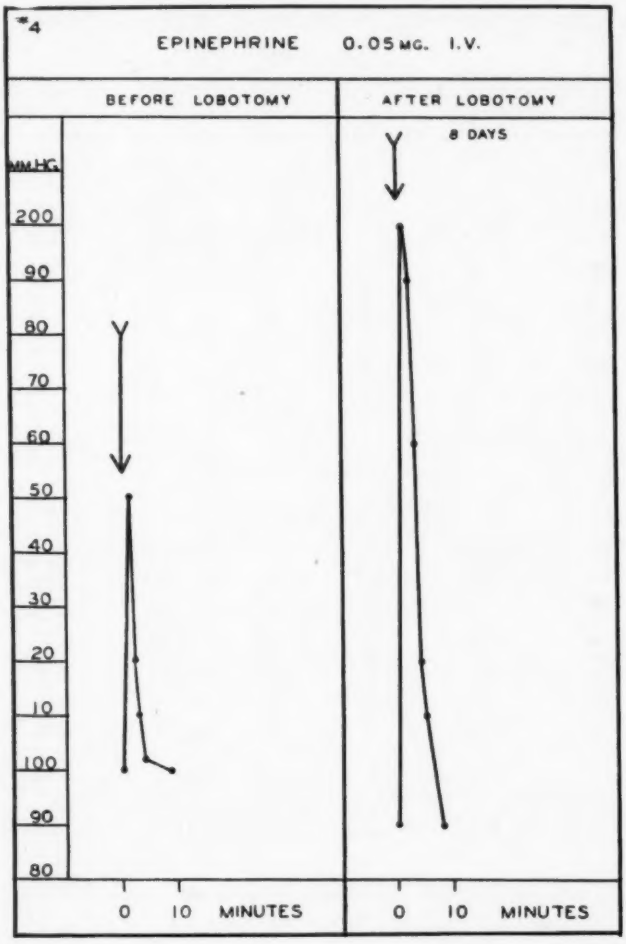

Fig. 1.—Responses to intravenous injection of 0.05 mg. of epinephrine hydrochloride before and after lobotomy. The arrow marks the point at which epinephrine was injected.

cats caused panting, increase in heart rate and increased production of epinephrine, as shown by the denervated iris and the nictitating membrane.

6. Kennard, M. A.: Autonomic Functions, in Bucy, P. C.: The Precentral Motor Cortex, Urbana, University of Illinois Press, 1944, p. 304.

In our patients, however, there was no blocking of the vagus nerve or elimination of vagal inhibition, as direct examination of the vagus system revealed.

Vagus or Parasympathetic Nervous System.—This system was tested by stimulation of the carotid sinus. Our experiments revealed a dramatic effect, consisting of three groups of reactions in sequence: (1) slowing of the heart to the point of cardiac arrest, (2) high voltage slow waves in the 2 to 5 per second range of frequency in the electroencephalogram

TABLE 2.—*Rise in Pulse Pressure of Patients With and Without Lobotomy on Intravenous Injection of 0.05 Mg. of Epinephrine Hydrochloride*

				After EST : IST *			
No.	Initial Pulse Pressure, Mm.	Height of Reaction, Mm.	D †	No.	Initial Pulse Pressure, Mm.	Height of Reaction, Mm.	D †
7	40	100	60	2	70	80	10
	50	80	30	3	60	60	0
	50	80	30	4	30	30	0
	70	100	30	5	30	70	40
	60	90	30	6	50	70	20
	50	80	30	9	40	60	20
	60	95	35	18	40	70	30
17	40	70	30	19	40	70	30
27	60	90	30				
	Average: 33.9 mm.				Average: 18.7 mm.		
	Total average: 26.3 mm. Hg ‡						
	Patients After Lobotomy						
No.	Initial Pulse Pressure, Mm.	Height of Reaction, Mm.	D †	No.	Initial Pulse Pressure, Mm.	Height of Reaction, Mm.	D †
1	40	90	50	20	30	140	110
	30	90	60	21	30	90	60
4	30	100	70	22	40	70	30
	30	120	90	26	80	110	30
	40	80	40	43	40	100	60
9	40	110	70	44	30	90	60
11	70	120	50	54	30	90	60
18	30	90	60	59	30	100	70
	Total average: 60.6 mm.Hg ‡						

* EST and IST indicate previous electric and insulin shock treatments.
† D is the difference between the basal and the highest pulse pressure.
‡ The total average refers to the difference between the basal and the highest pulse pressure.

and (3) loss of consciousness with tonic-clonic convulsions (figs. 3 and 4).

Patients Undergoing Lobotomy: Twenty-five such patients were compared with 40 control patients on whom no operation was performed. Table 3 shows that on stimulation of the carotid sinus the electrocardiogram recorded a positive effect in 84 per cent of the patients operated on, as compared with 63 per cent of the control group. Among those undergoing lobotomy, the incidences of a slight to moderate slowing of the heart (+ to ++) and very marked slowing or cardiac arrest (+++ to ++++) were about equal, i.e., 44 and 40 per cent, whereas for the control group the values were 40 and 22.5 per cent respectively.

From these figures, it can be seen that on stimulation of the carotid sinus in patients after lobotomy the incidence of a maximal cardiac reaction was about twice that for the control group. This observation permits the conclusion that in the patients operated on the vagus system responds readily to appropriate stimulation, in fact, more readily (84 as compared with 63 per cent) and with greater intensity (40, as compared with 22.5 per cent) than in the control group.

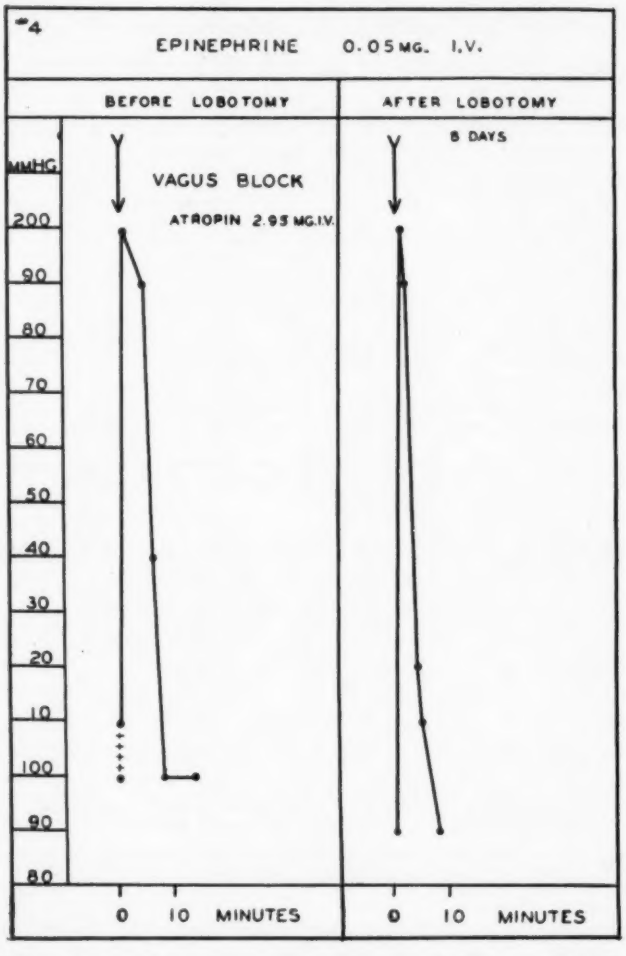

Fig. 2.—Rise in blood pressure on intravenous injection of 0.05 mg. of epinephrine hydrochloride after lobotomy, as compared with the effect on the blood pressure of a normal subject after block of the vagus nerve by intravenous injection of 2.95 mg. of atropine sulfate. The arrows mark the point at which the epinephrine was injected.

In 9 instances we were able to compare the effect of stimulation of the carotid sinus in the same patient before and after lobotomy. The results, as recorded in table 4, show that in all patients the carotid sinus

reflex became positive after lobotomy. Again, there was the intensified effect on the heart.

Observations, therefore, on the effect of stimulation of the carotid sinus in patients who have undergone lobotomy clearly reveal that in human subjects the severance of the frontal lobes neither eliminates nor blocks the vagus system.

Electroencephalographic recordings demonstrated that 92 per cent of the patients operated on had high voltage slow waves in the 2 to 5 per second range of frequency, as compared with 50 per cent for the control group. Also, the clinical signs, namely, loss of consciousness and

TABLE 3.—*Effect of Stimulation of the Carotid Sinus in Patients Who Have Undergone Lobotomy*

	Hospital Patients (No Operation)	Patients After Lobotomy
Number of patients	40	25
Electrocardiogram	25 (63%)	21 (84%)
Effect on heart rate *		
+ - ++	16 (40%)	11 (44%)
+++ - ++++	9 (22.5%)	10 (40%)
Electroencephalogram †	20 (50%)	23 (92%)
Clinical signs ‡	17 (42%)	22 (88%)

* + - ++ indicates slowing of the heart (increased QRS interval); +++ - ++++, heart arrest.
† Figures indicate the incidence of high voltage slow waves in the electroencephalogram.
‡ Clinical signs included unconsciousness and tonic-clonic convulsions.

TABLE 4.—*Effect of Stimulation of the Carotid Sinus on Nine Patients Before and After Lobotomy*

	Before Lobotomy	After Lobotomy
Electrocardiogram	5 (55.5%)	9 (100%)
Slowing of heart *		
+ - ++	5 (55.5%)	3 (33.3%)
+++ - ++++	0	6 (66.6%)
Electroencephalogram †	6 (66.6%)	9 (100%)
Clinical signs ‡	5 (55.5%)	9 (100%)

* + - ++ indicates slowing of the heart (increased QRS interval); +++ - ++++, heart arrest.
† Figures indicate the incidence of high voltage slow waves in the electroencephalogram.
‡ Clinical signs included unconsciousness and tonic-clonic convulsions.

short-lasting tonic-clonic convulsions, were more frequently observed in the patients undergoing lobotomy (88 per cent) than in the control group (42 per cent).

Control Group: To establish a control group, we examined 52 hospital patients who had not undergone lobotomy, but many of whom had received various forms of shock treatment. Since stimulation of the carotid sinus resulted in an unusually high percentage of positive reactions, we attempted to obtain normal controls by enlisting the cooperation of 14 medical students and nurses. Seven of these 14 subjects exhibited only slight electrocardiographic and electroencephalographic

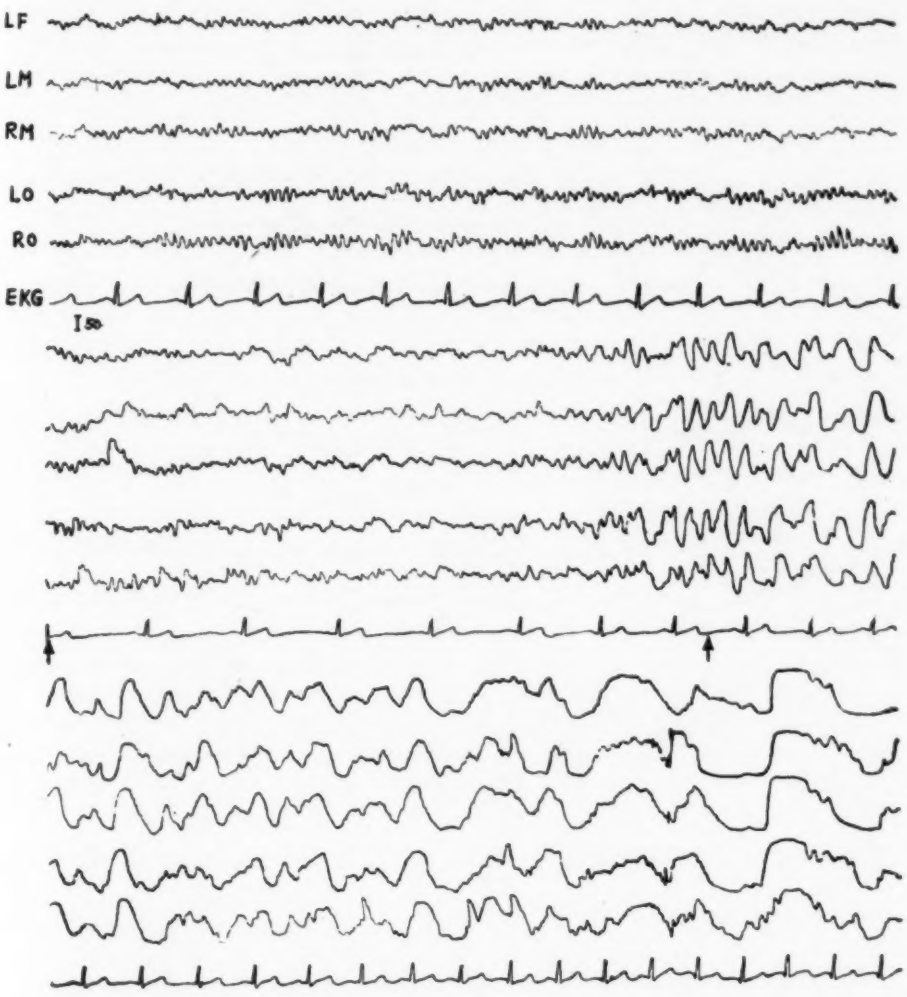

Fig. 3.—Continuous electroencephalographic and electrocardiographic recordings, with effects of bilateral stimulation of the carotid sinus.

The electroencephalographic leads are indicated as follows: *LF,* left frontal area; *LM,* left motor area; *RM,* right motor area; *LO,* left occipital area; *RO,* right occipital area.

EKG, indicates the electrocardiogram, with electrodes placed on the right and left sides of the upper part of the chest.

The upright marker indicates 50 microvolts. Each strip of record represents ten seconds.

The first arrow marks the beginning of stimulation of the carotid sinus; the second arrow, the end of stimulation and the beginning of convulsions, which lasted about twelve seconds. The electrocardiogram immediately after beginning of stimulation shows moderate slowing of the heart, which is followed by increased heart rate.

The electroencephalogram, about seven seconds after beginning of stimulation, shows high voltage slow waves, which appear from all cortical areas.

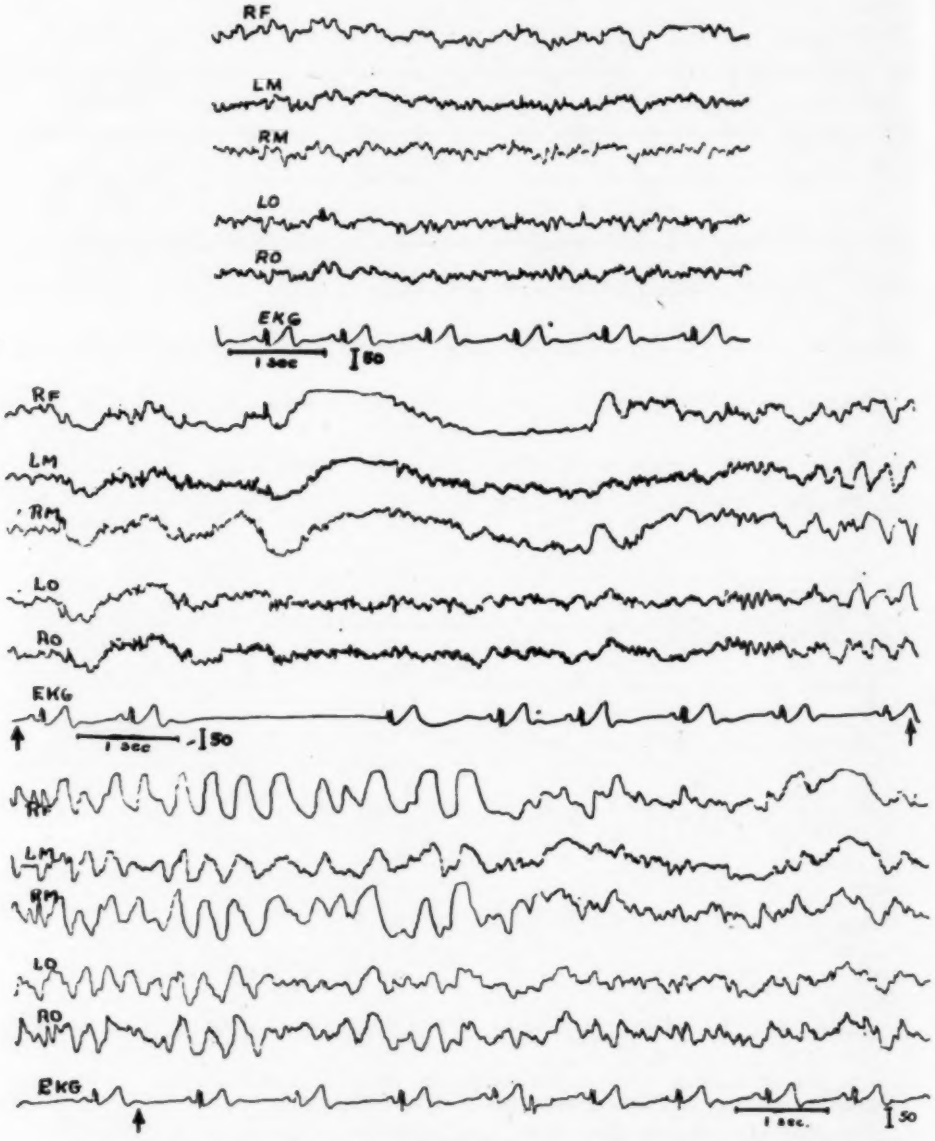

Fig. 4.—Continuous electroencephalographic and electrocardiographic recordings, showing effects of bilateral stimulation of the carotid sinus for ten seconds (interval between arrows).

The electroencephalographic leads are indicated as follows: *RF*, right frontal area; *LM*, left motor area; *RM*, right motor area; *LO*, left occipital area; *RO*, right occipital area.

EKG indicates the electrocardiogram, with electrodes placed on the right and left sides of the upper part of the chest.

The upright marker is equivalent to 50 microvolts; the horizontal marker to one second.

The first arrow marks, the beginning of stimulation of the carotid sinus; the second arrow, the end of stimulation, and the third arrow, the onset of convulsions. Immediately after beginning of stimulation, heart arrest occurred; about eight and one-half to nine seconds after stimulation high voltage slow waves arose from all cortical areas and at about eleven seconds tonic-clonic convulsions occurred, lasting about five seconds.

signs, just enough to demonstrate the presence of the reflex. The other 7 subjects, however, reacted on stimulation of the carotid sinus with tonic-clonic convulsions and loss of consciousness, and both the electroencephalogram and the electrocardiogram recorded abnormal responses. The history of each of these 7 volunteers revealed a preexisting pathologic condition, such as fainting spells and emotional instability. It was not surprising, therefore, to find a high incidence of positive carotid sinus reactions in a group of hospital patients with various mental diseases and a history of previous insulin, metrazol or electric shock treatment (table 5). Patients who had received shock treatment had a higher incidence of positive sinus responses than did untreated patients (table 5).

Table 5 shows that shock treatment enhances the effect of stimulation of the carotid sinus on both the control group of hospital patients and the patients who had undergone prefrontol lobotomy. The incidence

TABLE 5.—*Influence of Shock Treatment on Carotid Sinus Reflex*

	Hospital Patients (No Operation)		Patients After Lobotomy	
	Without Shock	With Shock	Without Shock	With Shock
Number of patients	19	21	9	16
Electrocardiogram *	11 (57.8%)	14 (66.6%)	6 (66.6%)	15 (93.7%)
+ - ++	6 (31.5%)	10 (47.6%)	3 (33.3%)	8 (50%)
+++ - ++++	5 (26.3%)	4 (19.0%)	3 (33.3%)	7 (43.7%)
Electroencephalogram †	6 (31.5%)	14 (66.6%)	7 (77.7%)	16 (100%)
Convulsions	5 (26.3%)	12 (57.1%)	7 (77.7%)	15 (93.7%)

* + - ++ indicates slowing of the heart (increased QRS interval); +++ - ++++, heart arrest.

† Figures indicate the incidence of high voltage slow waves in the electroencephalogram.

of a positive effect of stimulation of the carotid sinus in patients with mental disease and previous shock treatment was similar to that of patients with prefrontal lobotomy but without previous shock treatment. On the other hand, the combination of shock treatment and lobotomy brought up the incidence of positive carotid sinus reactions to almost 100 per cent, as indicated by convulsions and changes in the electrocardiogram and the electroencephalogram.

COMMENT

It has been demonstrated by many authors that the effects of stimulation of the carotid sinus are primarily parasympathetic. The observation that positive carotid sinus reactions were present in almost all the patients with prefrontal lobotomy leads to the conclusion that section of the frontal lobes liberates the parasympathetic, or cholinergic, system from cortical inhibitory influences, at least to some degree. The pharmacologic examination of the autonomic nervous system with epinephrine

uncovered a response of the sympathetic, or adrenergic, system which was similar to the effect of stimulation with epinephrine after vagal block. However, vagal block could not possibly have existed, since the overactive carotid sinus reflex indicated a greater excitability of the vagus system. This increased excitability of the vagus system pointed to liberation from cortical-autonomic-vagal inhibition. If this conclusion is correct, it must be assumed that there are in the frontal lobe cortical-vagal inhibitory centers.

The overreaction of the adrenergic system in patients undergoing lobotomy to direct stimulation with epinephrine indicates that the sympathetic system, too, is liberated from cortical inhibitory centers. This view is further substantiated by the clinical observation of outbursts of rage in some patients after section of the frontal lobe. These outbursts of rage resemble the phenomenon of sham rage in cats, inasmuch as they are associated with signs of excessive autonomic function which seem chiefly sympathetic in nature.

The question arises whether the overreaction of the sympathetic or of the parasympathetic nervous system is due to loss of inhibitory cortical control or to liberation of the one system from the counteraction of the other. On the basis of ingenious ablation experiments on cats, in which removal of the cortical representation of the autonomic system resulted in dramatic overreaction of the adrenergic system with the manifestation of the syndrome of "sham rage," Kennard [6] suggested that with the ablation of the frontal lobes the control of predominantly corticovagal centers was eliminated. However, in the monkey ablation of the frontal lobes does not lead to sham rage although similar signs of release of autonomic functions are observed. The predominance of adrenergic signs and the absence of observations on cholinergic signs in Kennard's experiments do not exclude the hypothesis that both the sympathetic and the parasympathetic nervous system are liberated from cortical inhibitory control. The absence of direct stimulation of the cholinergic system in Kennard's experiments complicates a comparison of her results with our observations on man. On direct stimulation, we found in man overreaction of both the sympathetic and the parasympathetic system, and, therefore, we arrived at the conclusion that this overreaction is due essentially to the loss of "cortical inhibition" of both the sympathetic and the parasympathetic system. This conception is in harmony with an opinion expressed by Langworthy [7] and associates that "the cortical function is one of control or regulation of the finer autonomic adjustments and that its absence removes 'inhibition' and results in over-reaction of spasticity."

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7. Langworthy, O. R.: Behavior Disturbances Related to Decomposition of Reflex Activity Caused by Cerebral Injury: An Experimental Study of the Cat, J. Neuropath. & Exper. Neurol. **3**:87, 1944; cited by Kennard.[6]

Reitman [5] suggested that in leukotomized patients there exists an increased resistance to drugs which upset the "autonomic equilibrium." Our observations, on the contrary, indicate a decreased resistance, or, in other words, an increased responsiveness of the autonomic nervous system to epinephrine, as well as other autonomic drugs which we have tested in a number of preliminary experiments.

Clinical observations, particularly with regard to the blood pressure, which will be reported in a separate paper, are strongly indicative that excitatory cortical-autonomic centers are also located in the frontal lobes. This is substantiated by reports in the literature. Since section of the frontal lobes interferes, of course, with the functioning of the cortical inhibitory, as well as excitatory, autonomic centers and their regulating influence on the autonomic nervous system, and since the patients show autonomic equilibrium postoperatively, it can be assumed that homeostasis establishes itself on a different level.

SUMMARY

The autonomic nervous system was examined in a control group and in a series of patients who had undergone prefrontal lobotomy. The sympathetic nervous system was tested pharmacologically with intravenous injection of 0.05 mg. of epinephrine hydrochloride (1 : 1,000). The parasympathetic system was examined by means of stimulation of the carotid sinus reflex. The effects were recorded with the electrocardiograph and the electroencephalograph, and the clinical manifestations were carefully noted.

Subcortical section of the frontal lobes interferes with inhibitory and excitatory autonomic centers in the cortex, resulting in overreaction of the autonomic nervous system to direct stimulation.

After frontal lobotomy autonomic equilibrium is eventually established at a new level and is brought about by readjustments of the autonomic system.

This work confirms other reports that cortical representations of the autonomic nervous system are located in the prefrontal area.

479 Commonwealth Avenue.

HYPERHIDROSIS

Study of a Case

ALICE J. PALMER, M.B.
SYDNEY, AUSTRALIA

ALMOST a century has passed since Claude Bernard,[1] in 1852. noted the vasodilatation which follows section of the sympathetic nerve supply to the side of the head. Ten years later, in 1862, Maurice Raynaud [2] described the disease of the extremities which has since borne his name. Since that time knowledge of the sympathetic nervous system, in both its normal and its abnormal state, has increased to the point where dysfunction not only can be recognized but can be treated and cured by sympathectomy.

There follows an account of the history, study and treatment of a patient exhibiting an abnormality of the sympathetic nerve supply to the extremities.

REPORT OF CASE

CLINICAL OBSERVATIONS

History.—A girl aged 18 years presented the symptoms of excessive sweating of her hands and feet, swelling of the fingers and blueness and coldness of all four extremities. The hyperhidrosis, which was the patient's chief complaint, had been present since childhood but had become definitely worse in the last four years. Droplets of sweat were left on the keyboard when she played the piano; writing at school examinations was made difficult by her wet hands, and the disability greatly interfered with her occupation as a trainee nurse. She stated that the hyperhidrosis was confined to the palms and soles, the amount of sweating from the rest of the body seeming to her quite normal. She had noticed that heat and emotional stress greatly accentuated her symptoms. The blueness and coldness of the fingers and toes had also been present since childhood. From the age of 12 she had had increasingly severe attacks of chilblains each winter. At first the accompanying swelling, blueness and coldness of the fingers disappeared with the onset of warmer weather, but for the last four years this return to normal had not occurred. The swelling was not present at all times; it was increased by any form of physical exertion or any extreme of temperature, either heat or cold. The hands were blue and cold at temperatures at which normal hands are warm and pink. Except for an increase in weight and mild mental lethargy, the patient

From the Department of Medicine, University of Sidney.

1. Bernard, C.: Sur les effets de la section de la portion céphalique du grand sympathique, Compt. rend. Soc. de biol. **25**:168, 1852.

2. Raynaud, A. G. M.: De l'asphyxie locale et de la gangrène symmétrique des extrémités, Paris, Rignoux, 1862, p. 177.

complained of no other symptoms. Her previous health record and her family history contained nothing relevant.

Examination.—The patient's general appearance was that of a normal adolescent girl. It was her hands which immediately arrested attention—droplets of sweat were literally dripping from the tips of her fingers. Moisture was present generally over the palms but was not perceptible on the dorsal surface. There was swelling of all the soft tissues from the wrist downward, particularly around the base of the fingers, which were firm and indurated on palpation. Over this area of greatest swelling the skin was a mottled purplish blue (fig. 1). The finger tips and the dorsum of the hands were bright pink. The hands were uniformly cold to the touch. The feet presented similar signs, though to a less extent. Other physical findings were normal, pulsation being present in the main arterial branches of the limbs.

Several features of this case precluded an outright diagnosis of Raynaud's disease, e.g., the severity of the hyperhidrosis and the presence of pronounced swelling. The cyanosis of the extremities was not definitely spasmodic, and there was never any associated pain. Accordingly, it was decided to carry out investigations to determine, if possible, the site of the abnormality causing the dysfunction of blood vessels and sweat glands and also to test possible therapeutic measures.

INVESTIGATIONS

Basal Water Loss.—EXPERIMENT 1.—Certain factors were known to produce hyperhidrosis, but the first question to be answered was whether excessive sweating occurred in the absence of specific stimuli. That is, was the basal activity of the sweat glands greater than normal? Also, of the body's total water loss under basal conditions, was an abnormal proportion contributed by the sweat glands of the palms and soles?

The continuous basal water loss from the body, the insensible perspiration, occurs at a constant rate for any one person and bears a relation to the basal metabolic rate. The normal loss varies from 17 to 21 Gm. per square meter of body surface per hour, with an average of 19.5 Gm. per square meter per hour.[3] The lungs and the skin are the sources of this loss of water, the loss through the skin being by the physical process of transpiration and the physiologic process of sweating.[4] Under controlled conditions of temperature and humidity, the insensible perspiration rate can be measured by the use of the sensitive Sauter balance. To answer the questions postulated in this experiment, the patient's insensible perspiration rate was measured in this way, the patient being in the basal state. The hands were then covered with rubber gloves and the feet with thick cotton socks to prevent evaporation. (Incidentally, this did not prevent sweating from the palms and soles, an important point, since a compensatory increase of water loss from the lungs would then have occurred.[5])

Results: The insensible perspiration rate with the hands and feet uncovered was 15 Gm., and the insensible perspiration rate with the hands and feet covered was 14.8 Gm., per square meter per hour. These results indicate that the total

3. Lippmann, A.: On the Insensible Perspiration and Its Clinical Significance, M. J. Australia **1**:569, 1942.

4. Kuno, Y.: Physiology of Human Perspiration, London, J. & A. Churchill, Ltd., 1934, p. 48.

5. Kuno,[4] pp. 53-55.

rate of water loss for the patient under basal conditions was certainly not excessive—in fact, it was less than normal. As to the proportional amount lost by sweating from the palms and soles, this, also, was not greater than normal.

Since, then, it was concluded that specific stimuli were necessary in order to produce the hyperhidrosis of which the patient complained, the next step was to investigate the effects of applying such stimuli.

At this stage some means of detecting the presence of sweat other than with the naked eye became necessary. The method chosen was that described by Minor,[6] which depends on the production of a colored compound from starch and iodine in the presence of moisture. A mixture composed of iodine, dilute alcohol and castor oil was painted on the skin, and over this was sprayed finely ground, thoroughly dried potato starch. In the presence of any moisture the grains of starch powder changed in color from white to a deep purple, a change which was readily discernible to the naked eye and to the camera.

Effects of Raising the Room Temperature

Room Temperature, C.	Mean Cutaneous Temperature of Hands, C.		Color of Hands		Sweating Reactions	
	Patient	Control	Patient	Control	Patient	Control
16 to 18	29.3 (84.7 F.)	34.0 (93.2 F.)	Purplish blue	Normal faint pink	None	None
19 to 21	30.0 (86.0 F.)	34.0	Purplish blue	Normal faint pink	None	None
21 to 23	30.3 (86.5 F.)	34.0	Purplish blue	Normal faint pink	None	None
23 to 25	30.7 (87.2 F.)	36.0 (96.8 F.)	Purplish blue	Normal faint pink	Small amount	None
25 to 28	30.8 (87.4 F.)	36.0	Purplish blue	Normal faint pink	Slight increase	None
28 to 30	30.8	36.0	Purplish blue	Normal faint pink	Moderate but not excessive	Small amount

Temperature readings of the skin were also required, and for this a sensitive dermotherm was used.

Heat and mental or emotional stress were the two most potent sudorific stimuli of which the patient complained; so the following experiments were carried out:

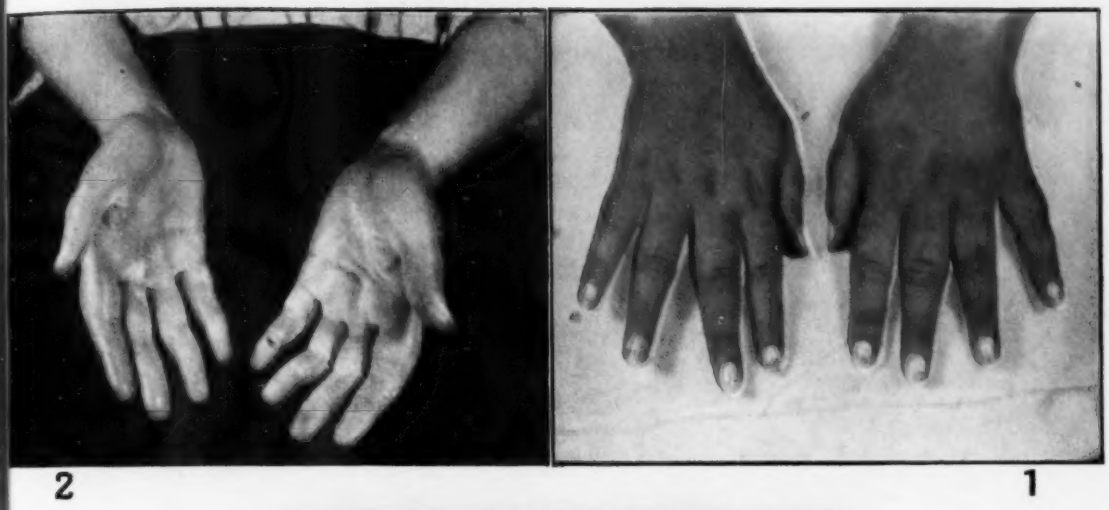
Effect of Heat.—Experiment 2.—The relative humidity being kept constant at 65 per cent, the room temperature was gradually raised from 16 to 30 C. The effects of this moderate increase in room temperature on the blood vessels and the sweat glands of the patient's hands were compared with those of a normal control.

Experiment 3.—The feet were immersed in a hot water bath at 48 C., and the effect on color and moisture of the hands was observed.

Experiment 4.—The hands were immersed in hot water at 48 C. to determine the effect of direct heat on the color and contour.

In experiment 2, the effect of raising the room temperature from 16 to 30 C. may be seen in the accompanying table. It will be noted that sweating commenced on the patient's hands at a room temperature of 23 C., as compared with 30 C.

6. Minor, V.: Ein neues Verfahren zu der klinischen Untersuchung der Schweissabsonderung, Deutsche Ztschr. f. Nervenh. **101**:302, 1928.



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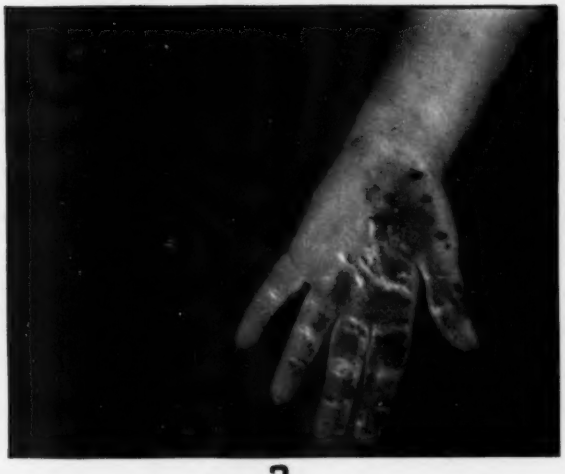

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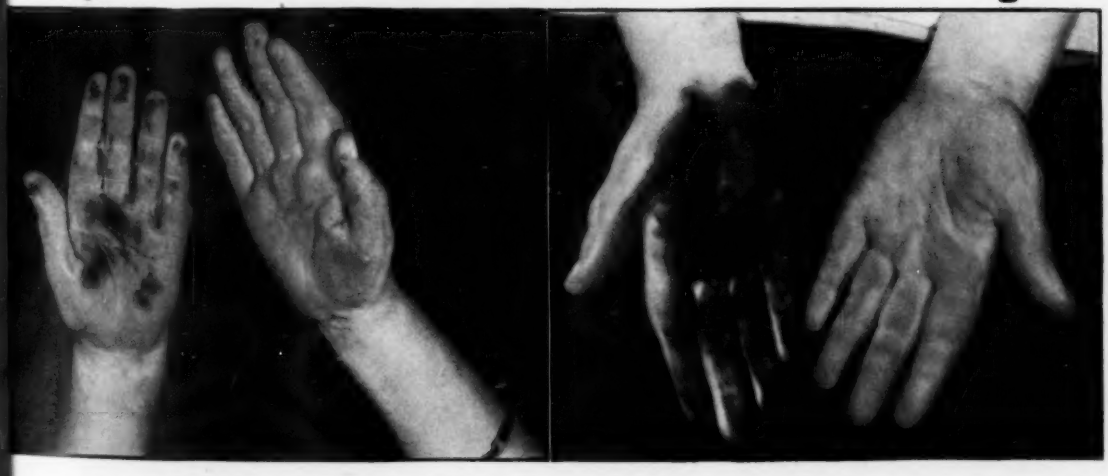

Fig. 1.—Hands before operation, showing bluish color and swelling around the proximal phalanges.
Fig. 2.—Inhibition of sweating over the area supplied by the ulnar nerve after blocking of the nerve.
Fig. 3.—Appearance of the left hand twenty-four hours after the first sympathectomy.
Fig. 4.—Appearance of the hands twenty-four hours after the second sympathectomy.
Fig. 5.—Absence of effect of mental stress on the sweat glands of the hands two years after operation.

for a normal control. The amount of sweating was also excessive. There was no significant rise in the cutaneous temperature of the patient's hands consequent on a rise of 14 C. in room temperature. At 30 C. the patient's hands were colder than those of the control at 16 C. Furthermore, the color of the hands remained purplish blue throughout the experiment.

In experiment 3, the hands were blue at the commencement of the experiment. During the next ten minutes the color gradually changed to a dull pink. The amount of sweating was sufficient to turn the starch to a confluent black layer.

In experiment 4, immediately the hands were placed in the hot water they turned bright pink, and the tissues around the proximal phalanges became greatly swollen. The sweating in experiments 2 and 3 was confined to the palms, there being no sweating perceptible on the dorsum.

Analysis of the results of these experiments reveals certain notable points in relation to the effect of heat on the blood vessels and sweat glands in this patient.

1. Vasoconstriction at low temperatures was more pronounced than in the normal hand. Moreover, it persisted up to rather high room temperatures. In contrast to this exaggerated vasoconstriction, the response to the direct heat of the water bath was an excessive vasodilatation. Thus, it would seem that adequate control of the peripheral vessels was lacking, but whether this was a local defect or whether the fault was in the nerve supply had still to be determined.

2. The response of the sweat glands to a rise in room temperature was precocious, occurring at lower temperatures of both room and skin than in the normal control. The distribution of the sweating was unusual, since in the normal person heat sweating occurs on the dorsum rather than the palm of the hand.[7] Finally, the degree of vasodilatation and the activity of the sweat glands did not run parallel with one another; the one was delayed, whereas the other was precocious.

Effect of Mental Stress.—EXPERIMENT 5.—The patient was seated in a quiet, cool room alone with the observer. She was plied with problems in mental arithmetic. Sweating commenced on the palms within two minutes and rapidly increased to an excessive amount as compared with that in a normal person tested under the same conditions. It was interesting to note that there was no hyperhidrosis in the axillary region, which is a normal site for mental sweating.

Effect of Sudorific Drugs.—EXPERIMENTS 6 AND 7.—To complete the study of the effects of sudorific stimuli, it now remained to administer the two drugs, pilocarpine nitrate (experiment 6) and methylcholine chloride U.S.P. (acetyl-beta-methylcholine chloride; "mecholyl chloride") (experiment 7). In each case the dose was 10 mg., given hypodermically. The effect of the drugs, not only on localized areas of sweat glands but on the total water loss from the body, was studied. The latter was done by use of the Sauter balance, which measured the progressive loss of weight due to evaporation of water from the body surface. The same dose of pilocarpine nitrate was subsequently administered to a group of medical students as a guide to the total water loss to be expected in a normal person.

The results are best shown in graphic form (fig. 6). It will be seen that both the rate and the total amount of water loss from the patient were greater than in the normal controls, but not strikingly so. The normal controls varied widely among themselves. There was copious sweating from the patient's hands and feet, the starch being changed from white to a confluent blackness. Sweating

7. List, C. F., and Peel, M. M.: Sweat Secretion in Man, Arch. Neurol. & Psychiat. **39**:1228 (June) 1938.

from the hands and feet of the normal controls was somewhat less in amount. Therefore it seems that the greater total amount lost by the patient could be explained by the localized excessive sweating of the hands and feet, and there was no need to postulate a hypersensitivity of the whole sweating mechanism to sudorific drugs.

Peripheral Nerve Block.—Hitherto, all the experiments had been designed to effect a stimulation of the sweat glands. The next step was to seek means of inhibiting them, particularly with a view to forecasting the effect of sympathectomy.

EXPERIMENT 8.—The sympathetic fibers supplying the vessels and sweat glands of the hands are carried in the main peripheral nerves. Of these, the ulnar nerve is readily accessible at the elbow, offering a convenient site for anesthetization.

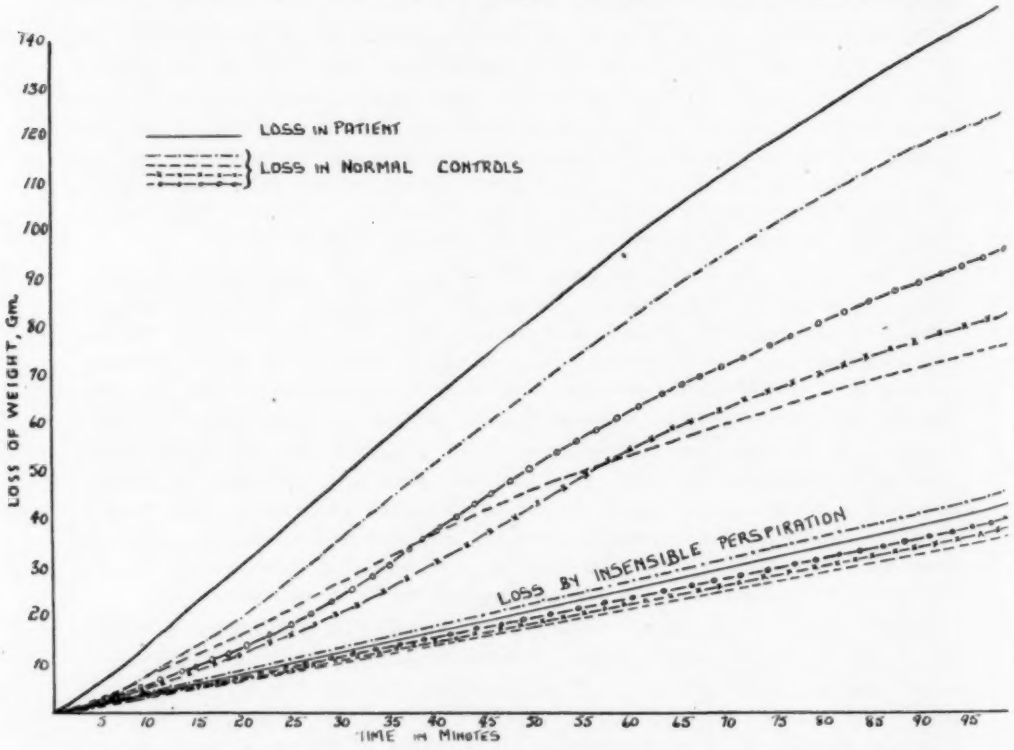

Fig. 6.—Patient's response to pilocarpine as compared with the response of normal subjects.

On two occasions 6 cc. of dibucaine ("nupercaine" or "percaine") hydrochloride with epinephrine hydrochloride was injected into the patient's right ulnar nerve, 1 cc. intraneurally and 5 cc. perineurally. On the first occasion sweating reactions were observed. The sweating was spontaneous, no additional sudorific stimulus being necessary. Less than ten minutes after the anesthetization, the right palm presented a striking picture, the effect resembling a textbook diagram of the distribution of the cutaneous nerves in the palm. A distinct line running down the center of the third finger and continuing across the palm divided the blackened, radial side from the white, ulnar side (fig. 2). The complete inhibition of sweating over the ulnar area lasted three hours.

The purpose of the second anesthetic was to study the vascular reactions and take readings of the cutaneous temperature. Vasodilatation was soon obvious over the ulnar area and persisted for several hours. An interesting phenomenon was seen on the radial side of the palm. For the first fifteen minutes the vessels remained constricted; then there was a gradual vasodilatation until the cutaneous temperature was finally as high as that on the ulnar side. The left hand, meanwhile, showed persistent vasoconstriction. The most likely explanation of this phenomenon seems to be the gradual diffusion from the ulnar to the radial side of the palm of some chemical vasodilatory substance. The results of this experiment are shown in figure 7.

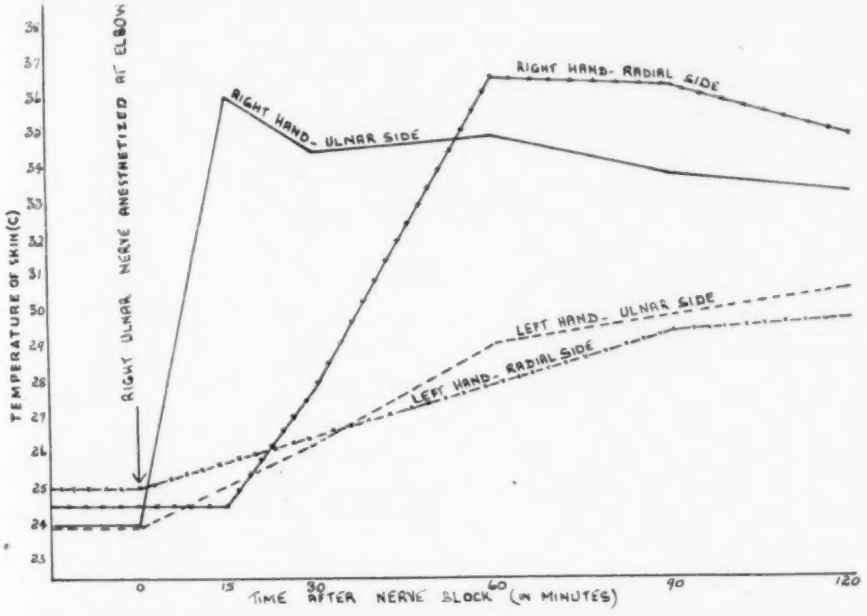

Fig. 7.—Effect of ulnar nerve block on the cutaneous temperature of the hand. Each point plotted on the graph is the mean of readings from eight specified points on the palm and the dorsum of the hand.

SYMPATHECTOMY

When the ulnar nerve block proved to be effective in relieving the patient's symptoms, sympathectomy was indicated as a more permanent form of treatment. The preganglionic type of operation was performed, the dorsal sympathetic chain being severed between the third and the fourth thoracic ganglia, first on the right side and three weeks later on the left. A lumbar sympathectomy for the relief of symptoms in the feet was not considered necessary, as these were of a much milder nature.

Postoperative Studies.—Twenty-four hours after the first operation, the treated (right) hand was warm, dry and pink. The untreated (left) hand was cold, dripping sweat and blue in color. The result of applying iodine and starch at this time may be seen in figure 3. The average difference in temperature between the two hands was 8 degrees (C.) [14.4 degrees (F.)]. Similar observations were made three weeks later, i. e., twenty-four hours after the second sympathec-

tomy and then on the fifteenth and thirtieth days of the postoperative period. The average temperature on each of these occasions is shown in figure 8. It is significant to note the slight fall by the fifteenth day, followed by a return to the immediate postoperative level by the thirtieth day. As to the sweating reactions, twenty-four hours after the second operation the left hand was completely dry, but a small amount of sweating was present on the palm of the right hand (fig. 4). On the fifteenth and thirtieth postoperative days both hands gave a slightly positive reaction to the iodine and starch test.

Effect of Heat, Mental Stress and Pilocarpine.—It was obvious that the patient's symptoms had been greatly alleviated by the sympathectomy, at least while she remained at rest. What would, now, be the effect of heat, mental stress and sudorific drugs?

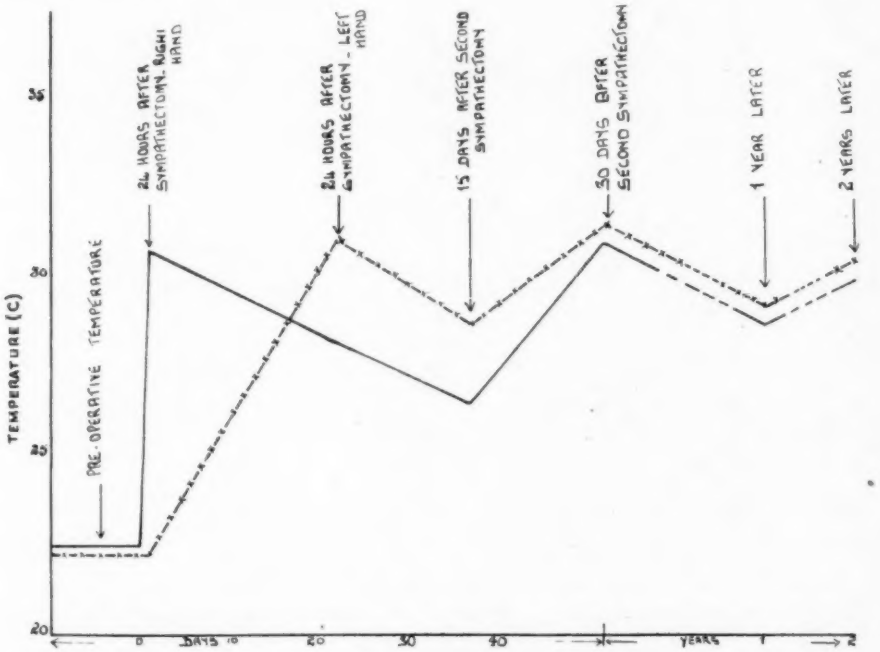

Fig. 8.—Changes in mean temperatures of the hands after sympathectomy. Values for the right hand are indicated by the solid line; values for the left hand, by the line of crosses and dashes.

To answer these questions, experiments 3, 5 and 6 were repeated in the fifth week of the postoperative period. Immersing the feet in water heated to 48 C. resulted in a rise of 3 degrees (C.) [5.4 degrees (F.)] in the average temperature of the hands. There was some sweating—enough to cause a patchy color change in the layer of starch, but a very small amount as compared with the confluent blackness of the preoperative experiment. Similarly, mental stress caused a much diminished amount of sweat to appear on the palms. When 10 mg. of pilocarpine nitrate was injected, the sweating of the palms was as copious as in the preoperative experiment.

Later Result of Operation.—Two years have passed since the sympathectomy was performed; so when the patient was seen recently, it was possible to gain

some indication of whether the immediate postoperative relief from her symptoms was to be only temporary or whether it was likely to be of a more permanent nature. It was found that the condition of her hands had improved even further. Despite its being midwinter, they were pink and quite dry and warm, their average temperature being 2 degrees (C.) [3.6 degrees (F.)] higher than that of a normal control. Swelling around the proximal phalanges had diminished but was still noticeable. Heat sweating and mental sweating were within normal limits. A final experiment was performed.

EXPERIMENT 9.—The right ulnar nerve was anesthetized at the elbow, and cutaneous temperatures and sweating reactions were observed. It was found that no rise of temperature occurred over the anesthetized area; i. e., there was no further vasodilatation. No sweating was visible on any part of the hands. Ten milligrams of pilocarpine nitrate was then injected hypodermically into the left arm. Within two minutes copious sweating broke out on the face and trunk. In contrast to the previous two occasions on which pilocarpine had been administered, only a minimal amount of sweating appeared on the hands, hardly more than could be accounted for by the stress of the injections and the heat of the photographic lamps. There was no difference between the anesthetized right ulnar area and the rest of the hands.

COMMENT

The purpose of the investigation in this case was to determine, if possible, the underlying cause and nature of the malady and to forecast the benefit likely to accrue from sympathectomy.

First, what was the site of the lesion? There were several possibilities—a local defect in the blood vessels and sweat glands or a defect in the sympathetic nervous system, either in its peripheral portion or centrally, as in the hypothalamus or the premotor cortex. A local fault seems the least likely explanation. Lewis [8] brought forward much evidence in favor of a local hypersensitivity to cold being the basis of symptoms in Raynaud's disease. This might explain the vascular phenomena in the present case but would not explain the hyperhidrosis which was such a prominent feature. Also, a local defect would not account for the effectiveness of the sympathectomy in relieving the symptoms.

The control of vasomotor tone and the control of sweat gland activity are both functions of the sympathetic nervous system, and it seems likely that the fault lay either in the peripheral or in the central portion of this system. The theory of a postganglionic site as the origin of the hyperactivity is discredited by the success of the preganglionic operation. The theory of a central origin is supported by several points—the symmetric distribution of the symptoms, the involvement of all four limbs and the response to reflex stimuli, such

8. Lewis, T.: Experiments Relating to the Peripheral Mechanism Involved in Spasmodic Arrest of the Circulation in the Fingers: A Variety of Raynaud's Disease, Heart **15**:7, 1929.

as that of the hands to heating of another portion of the body. The potent effect of psychic stimuli in provoking the symptoms, as well as the tendency to obesity which became manifest concurrently with the increase in severity of the sweating and vascular symptoms, suggests a central disorder. Whether the premotor cortex or the hypothalamus was primarily at fault it is not possible to say. The sweating disturbance in this case is similar to that described by Adson, Craig and Brown in their cases of "essential hyperhidrosis."[9]

The next question to be decided is whether the defect was purely functional or whether the symptoms could have resulted from an organic lesion. The latter seemed quite possible at one stage, for in the attempt to expose the dorsal portion of the sympathetic chain in the first operation an abnormally dense plexus of veins was observed closely surrounding it. Could pressure from this plexus be the cause of the patient's symptoms? The answer to this question was in the negative, because the symptoms were bilateral and the second operation revealed no abnormal venous plexus on the other side. No evidence of any other organic lesion was seen; so one must conclude that the derangement was one of function, and not of structure. What caused the localized dysfunction is obscure. There was no history of infection, such as encephalitis, no trauma or nutritional disease and nothing in the family history to suggest a genetic factor. A congenital anomaly of the sympathetic nervous system is the only satisfactory explanation, and the fact that the symptoms dated from childhood lends weight to this theory.

During the investigations several observations were made which are worthy of note. The distribution of heat sweating on the hand was unusual. Instead of its being confined to the dorsum, leaving the palms relatively free, the palms sweated copiously, whereas no moisture was discernible on the dorsum.

The response to pilocarpine was interesting on the three occasions on which the drug was given. Before operation, and one month after sympathectomy, the drug stimulated the sweat glands of the hands to great activity. On the third occasion, two years later, the response was negligible and, moreover, was not affected by the ulnar nerve block. The site of action of pilocarpine is thought to be directly on the effector cells, and not on nerve fibers or nerve endings;[10] so one

9. Adson, A. W.; Craig, W. McK., and Brown, G. E.: Essential Hyperhidrosis Cured by Sympathetic Ganglionectomy and Trunk Resection, Arch. Surg. **31**:794 (Nov.) 1935.

10. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941, p. 391.

would not expect sympathectomy to alter the response to the drug. If this theory of the site of action is correct, a possible explanation for the lack of response on the third occasion is that the sweat glands of the hands had atrophied as a result of interruption to the central connections of their nerve supply. This would be an atrophy due to disuse, not the atrophy resulting from cutting the immediate fibers supplying the glands, for these postganglionic fibers are left intact by the preganglionic operation. Such an explanation is not invalidated by the fact that the second occasion was also in the postoperative period, for it was then but a month after the operation and the sweat glands would not have atrophied sufficiently to prevent them from responding to a direct stimulus. Also, at this stage one would expect a strong, positive reaction to a parasympathomimetic drug such as pilocarpine because of the so-called sensitization phenomenon. This response was first noted in connection with the effect of epinephrine on the ear vessels of a rabbit after sympathectomy.[11] The nerve endings to the sweat glands are cholinergic and are therefore hypersensitive to parasympathomimetic drugs, although they are part of the sympathetic system. The postganglionic type of operation renders the patient much more liable to this sensitization phenomenon, and the preganglionic operation was designed to avoid it. Nevertheless, it still occurs, though to a much less extent.

The dramatic complete relief from symptoms for the first four to five days after operation and their gradual partial return for a limited period was not a unique phenomenon in this patient. It has often been observed to follow sympathectomy for peripheral vascular disorders.[12]

In conclusion, it seems from present indications that the patient has a fairly good chance of enjoying permanent relief from her symptoms. Two years after operation, there are no signs of nerve regeneration, and her hands are as warm, dry and pink as those of a normal person.

SUMMARY

A girl gave a history suggestive of Raynaud's syndrome but presenting unusual features.

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11. Meltzer, S. J., and Meltzer, C.: The Share of the Central Vasomotor Innervation in the Vasoconstriction Caused by Intravenous Injection of Suprarenal Extract, Am. J. Physiol. **9**:147, 1903; On the Effects of Subcutaneous Injection of the Extract of the Suprarenal Capsule upon the Blood Vessels of the Rabbit's Ear, ibid. **9**:252, 1903.

12. White, J. C., and Smithwick, R. H.: The Autonomic Nervous System, London, The Macmillan Company, 1942, p. 174.

Investigations were carried out to study the effect of heat, mental stress, sudorific drugs and peripheral nerve block on the sweat glands and the blood vessels of the hands.

A preganglionic dorsal sympathectomy was performed.

The preoperative experiments were repeated, and the patient's symptoms were found to be greatly relieved.

The site and nature of the disorder and its etiologic factors are discussed, and mention is made of several interesting points observed during the investigations.

Prof. C. G. Lambie permitted the investigations on this patient, who was under his care. Dr. Ivor Hotten performed the peripheral nerve blocks, and Dr. A. Lippmann and Mr. M. J. Morrissey cooperated in several of the experiments. Dr. S. Woodward-Smith made the color photographs. The operation of sympathectomy was performed by Dr. Gilbert Phillips.

University of Sydney.

SPINAL EXTRADURAL CYST

Report of a Case, with Particular Reference to a Possible Diagnostic Aid

OSCAR A. TURNER, M.D.
YOUNGSTOWN, OHIO

THE INTEREST in noninflammatory and non-neoplastic cysts of the spinal extradural space was initiated by the report of Elsberg, Dyke and Brewer [1] in 1934. They described 4 cases of such a cyst encountered among 250 tumors of the spinal cord and evolved a clinical and roentgenologic syndrome which has proved to be diagnostic of the condition. They described the combination of signs and symptoms as follows:

> The individual is an adolescent with the history of symptoms of a progressive spastic paraplegia. Pain is absent or is not a prominent symptom. The objective disturbances of sensibility are slight and their upper level is in the mid-thoracic dermatome. The manometric tests demonstrate a subarachnoid block with the characteristic spinal fluid changes of cord compression. Measurements on antero-posterior x-ray films show that the interpedicular spaces of three or more vertebrae are enlarged. The pedicles of the affected vertebrae, especially those of the sixth, seventh, and eighth, are narrowed and atrophic.

Cloward and Bucy,[2] in 1937, first recognized the association of the condition known as vertebral epiphysitis, or Scheuermann's disease,[3] with the presence of spinal extradural cyst and thus added another component, kyphosis dorsalis juvenilis, to the syndrome described by Elsberg, Dyke and Brewer.[1] The literature pertaining to this cyst and the associated changes in the spinal column was reviewed by Adelstein [4] in 1941, who reported an additional case, bringing the total recorded in the literature at that time to 17 cases. Since this review other cases have been described, and in table 1 are listed the cases reported since 1941. However, a case reported by Collins and

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From the Neurosurgical Service and the Neuropathologic Laboratories of the Jewish Hospital of Brooklyn, Brooklyn.

1. Elsberg, C. A.; Dyke, C. G., and Brewer, E. D.: The Symptoms and Diagnosis of Extradural Cysts, Bull. Neurol. Inst. New York **3**:395-417, 1934.

2. Cloward, R. B., and Bucy, P. C.: Spinal Extradural Cysts and Kyphosis Dorsalis Juvenilis, Am. J. Roentgenol. **38**:681-706, 1937.

3. Scheuermann, H.: Kyphosis dorsalis juvenilis, Ztschr. f. orthop. Chir. **41**: 305-317, 1921.

4. Adelstein, L. J.: Spinal Extradural Cyst Associated with Kyphosis Dorsalis Juvenilis, J. Bone & Joint Surg. **23**:93-101, 1941.

Marks [5] had not been previously included in the collective review on the subject but was noted by Hamby [6] in his review of intraspinal tumors in childhood. It is to be noted that Mayfield and Grantham [7]

TABLE 1.—*Cases of Extradural Cyst Reported Since 1941*

Case No.; Date Reported	Author	Age	Duration of Symptoms	Sex; Race	Location of Cyst	Dilatation of Spinal Cord	Results and Comment
18 1915	Collins and Marks [5]	15*	4 yr.	F W	T 3-6	?	Complete neurologic recovery; no opening into subarachnoid space
19 1939	Turnbull [11]	14	3 mo.	F W	T 8-10	Present	Complete recovery; patient treated for tuberculosis on first admission; operation 4 yr. after onset of symptoms
20 1940	Meredith [12c]	41	8 mo.	M W	C 7, chiefly on right	?	Complete recovery; previous injury to cervical part of spine; possible traumatic origin
21 1942	Mayfield and Grantham [7]	16	3 yr.	M W	T 6-9	None †	Complete recovery; symptoms followed injury; remission in symptoms for 1 yr.
22 1942	Mayfield and Grantham [7]	26	12 yr.	M N	T (5) 6-8	Present† T 6-7	Practically complete recovery; history of 4 distinct remissions
23 1944	Good, C. A.; Adson, A. W., and Abbott, K. H.: Am. J. Roentgenol. **52**: 53-60, 1944	42	8 yr.		T 8-L 1	Present†	Radiopoque oil demonstrated in cyst before and after removal
24 1945	Shenkin, H. A.; Horn, R. C., and Grant, F. C.: Arch. Surg. **51**: 125-146, (Oct.) 1945	51	3 mo.	F	T 7-9	Present T 7-9	Complete recovery; tumor attached to T 9 root, measured 6 by 2.5 by 2.5 cm.; no cell lining layer
25	.....	13	2 yr.	F	T 6-8	Present	Complete recovery; no attachment to surrounding structures; development of kyphosis postoperatively
26 1945	Cohen, I.: J. Mt. Sinai Hosp. **12**: 116-118, 1945	48	3 mo.	F	T 8	Pedicle destroyed†	Results questionable; extradural neuroblastoma (sympathicoblastoma) at C 10 also present
27 1946	Turner	11	5 mo.	M W	T 10	Present†	Complete recovery

* Age at time of the first admission to the hospital.
† Dilatation as seen in the roentgenogram.

5. Collins, J., and Marks, H. E.: Early Diagnosis of Spinal Cord Tumors, Am. J. M. Sc. **149**:103-112, 1915.

6. Hamby, N. B.: Tumors in the Spinal Canal in Childhood: An Analysis of the Literature with Report of a Case, J. Nerv. & Ment. Dis. **81**:24-42, 1935.

7. Mayfield, F. H., and Grantham, E. G.: Spinal Extradural Cysts, Surgery **11**:589-595, 1942.

did not consider the cases reported by Schlesinger [8] and by Krause [9] as verified instances of extradural cyst. A total of 27 cases have been reported up to the present time. This does not include the case of Blum,[10] discovered in the literature by Cloward and Bucy [2] and noted by Mayfield and Grantham [7] as probably being one of extradural cyst.

It is generally recognized that in the presence of a complete or an incomplete subarachnoid block due to an intraspinal tumor withdrawal of spinal fluid from the subarachnoid space below the lesion may result in aggravation of already existing symptoms or signs. In such instances, a partial block may become complete; motor power may be further diminished, and changes in sensibility may become more pronounced. This has been interpreted as due to further impaction of the tumor against the already compressed cord, and in unusual cases acute compression of the cord may occur. Such changes are prone to occur oftener in the presence of movable growths, such as the perineural fibroblastoma, than with a fixed or sessile tumor, such as the meningioma or the intramedullary glioma. More frequently, however, removal of spinal fluid from below the site of the tumor, or increase in pressure of the fluid above the tumor, such as occurs in the determination of the spinal fluid dynamics, is associated with little change in the symptoms or physical signs other than increase in pain in the distribution of the involved posterior nerve roots if such pain is already present. Improvement in the clinical picture is still more unusual, and in the case reported here there was striking improvement in the motor power of the paralyzed lower extremities after removal of spinal fluid. This has never previously been noted in connection with extradural cysts, although Turnbull [11] was able to demonstrate recurrence of symptoms with activity following improvement as a result of prolonged rest in bed.

REPORT OF CASE

History.—An 11 year old boy, of Italian parents, was admitted to the hospital on Jan. 29, 1941, with the complaint of progressive loss of motor power in both lower extremities over a period of five months. The family history was essentially noncontributory, and the patient was one of 7 children, the ages of the siblings ranging from 14 to 28 years. He had a normal spontaneous birth at full term, and the neonatal period had been uneventful. There was a history of pneumonia in infancy and of asthmatic attacks with respiratory embarrassment every two to

8. Schlesinger, H.: Beiträge zur Klinik der Rückemarks-und Wirbeltumoren, Jena, Gustav Fisher, 1898, p. 46; cited by Adelstein.[4]

9. Krause, W. C.: A Case of Cyst Within the Spinal Canal, Brain **30**:533, 1907; cited by Adelstein.[4]

10. Blum, W.: Rückenmarksläsion bei Scheuermann'scher Krankheit (Kyphosis dorsalis adolescentium), Schweiz. med. Wchnschr. **66**:283-285, 1936.

11. Turnbull, F.: Spinal Extradural Cyst, Canad. M. A. J. **41**:250-253, 1939.

three months since the age of 5 years. There was no history of rickets or dietary deficiency.

The child had been well until late in August 1940, at which time it was noted that he began to drag the legs in walking. About two weeks after this it was observed that he fell frequently. The difficulty in gait progressed to total incapacitation, and he had been confined to bed for a month prior to admission to the hospital. At the time of his admission voluntary movements of the lower extremities were reduced to a minimum, but he had not been aware of sensory changes or paresthesias. The rectal sphincter had not been affected, but for about a month there had been difficulty in starting the urinary stream.

Examination.—The boy was well developed and slightly obese and did not appear ill. There was spastic paraplegia, with only minimal voluntary movement present in the lower extremities. Occasional spontaneous flexor spasms were present, particularly after painful stimulation. There was well sustained ankle and patellar clonus bilaterally, associated with pronounced hyperreflexia of the lower extremities. Plantar stimulation resulted in an extensor toe response, stronger

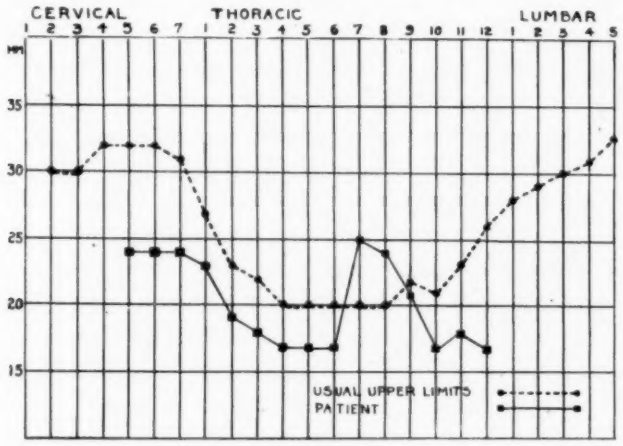

Fig. 1.—Graph showing the localized erosion of the pedicles of the seventh and eighth thoracic vertebrae. Normal measurements are from Elsberg and Dyke (Bull. Neurol. Inst. New York **3**:359-394, 1934).

on the left side than on the right. The Gordon-Oppenheim sign was present bilaterally, and there was a strongly positive suprapubic adductor sign. The abdominal reflexes were absent, and there was a positive Beevor sign, with conspicuous upward deviation of the umbilicus on raising the head against resistance. Sensory examination disclosed a sharp sensory level at the ninth thoracic dermatome with a narrow band of hyperesthesia on the left. On the left side sensation was practically absent, while on the right side the sensory loss was less complete. The sensory defect was for all modalities, although the temperature sense was less involved than was the pain or touch sense. The loss of position and vibration sensation was complete. There was possibly less impairment of sensation over the scrotum than in the adjacent regions. No evidence of kyphosis or any other spinal deformity was present.

Roentgenographic examination of the thoracic portion of the spine revealed notable enlargement of the canal, chiefly in the region of the seventh and eighth thoracic vertebrae. There were erosion and atrophy of the pedicles, as well as

erosion of the posterior margins of the bodies of the affected vertebrae (fig. 1). Lumbar puncture revealed an initial pressure of 170 mm. of water, which dropped to 135 mm. after the removal of 1 cc. of spinal fluid. The application of pressure up to 80 mm. of mercury by means of a cuff around the neck caused no change in the intraspinal pressure, demonstrating the presence of a complete subarachnoid block. The first cubic centimeter of fluid removed was slightly xanthochromic, whereas the remainder was colorless. The release of 4 cc. of fluid reduced the intraspinal pressure to 45 mm. of water. The fluid contained 4 lymphocytes per cubic millimeter and 67 mg. of total protein per hundred cubic centimeters. Examination of the patient immediately after the withdrawal of spinal fluid disclosed no change in the sensory status, although there was striking improvement in the motor power of the lower extremities. An hour and a half later the patient was able to lift either leg completely off the bed, and he had more motor power in the legs than had been present for many months prior to hospitalization. No pain was associated with the withdrawal of the spinal fluid.

Operation.—Operation disclosed the presence of a large extradural cyst, which was completely exposed only after the laminas of the sixth to the eleventh thoracic

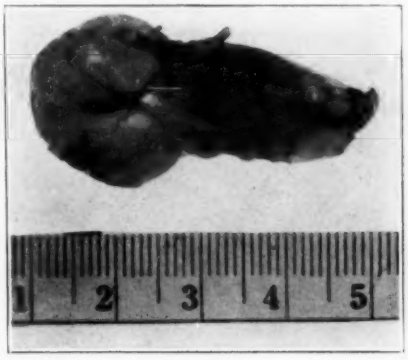

Fig. 2.—The intact cyst after removal at operation. The clip indicates site of the pedicle.

vertebrae had been removed. It was necessary to remove a portion of the articular facets to expose completely the lateral margins of the cyst. This was done so that a careful search could be made for extensions of the wall of the cyst along the nerve roots. The wall was thin and translucent; and, although it was adherent to the nerve roots, it could be demonstrated with certainty that no extensions were present. At the time of exposure, the cyst was rather tense, and, while aspiration of 10 cc. of clear, colorless fluid caused considerable relaxation of the wall of the cyst, fifteen minutes later the fluid had been replaced and the cyst had again become tense. Dissection of the cyst from the adherent structures exposed a pedicle 1 cm. in diameter which passed through a defect in the dura at one point about 5 mm. above the site of exit of the eighth thoracic root on the right side. It was certain that the cyst represented a herniation of the leptomeninges through the dural defect, and removal of the cyst by transection of the pedicle left an opening through which spinal fluid drained and the uncovered cord could be seen. The defect was closed with several interrupted silk sutures.

Postoperative Course.—Convalescence was uneventful, and progressive improvement followed removal of the cyst. At the time of discharge from the hospital

the patient was able to walk. Two weeks after operation perception of touch, pain and temperature had returned to normal, although there was still some impairment of vibration and position sense. To prevent the development of a spinal deformity, the patient was fitted with a body cast, which was later replaced with a form-fitting brace.

Pathologic Study.—The cyst measured 6 by 1.5 cm. The external surface was gray, smooth and glistening in some areas, while elsewhere it was roughened by yellowish gray tags of adherent tissue. In the central portion was an opening 8 mm. in diameter, at which point the pedicle had been attached. Loosely adherent to the pedicle side of the cyst were several moderate-sized vessels and a small segment of nerve root (fig. 2). The inner surface of the cyst was smooth, gray and dull, and without evidence of tumor nodule or gross inflammatory change.

Microscopically, the wall of the cyst was composed of a double layer of rather heavy collagenous tissue, which was partly hyalinized. An occasional flattened cell could be recognized on the inner surface. Between the inner and outer connective tissue layers forming the wall of the cyst was a layer of tissue formed either by a bank of cuboidal or flattened cells or by a mesh of elongated and stellate cells with interlacing processes. Sections of the nerve root and epidural fat were not unusual.

COMMENT

Several explanations have been offered to account for the origin of the spinal extradural cyst, and attention has centered generally on the suggestion of Elsberg, Dyke and Brewer [1] that it arises either as a congenital diverticulum of the dura mater or as a herniation of the arachnoid through a dural defect. No explanation has been offered, however, for the constant location of this cyst in the thoracic region. The suggestion that it is the result of herniation of the arachnoid has been favored by many authors, and there is much to support this view. Free communication between the cyst and the subarachnoid space was demonstrated by Mayfield and Spurling,[12] by Kelly [13] and by Cloward and Bucy.[2] On the basis of the microscopic appearance of the cyst, the last-mentioned authors favored the theory of origin from a dural diverticulum, as did Robertson and Graham.[14] In this respect, it is of interest that of the 27 cases reported in the literature to date, in only 3 [15] was there any significant history of trauma related to the occurrence of symptoms. In the case reported here, the evidence in favor of herniation of the arachnoid was quite definite, and a characteristic pedicle passing through a sharply delimited dural defect could

12. Mayfield, F. H., and Spurling, R. G., cited by Cloward and Bucy.[2]

13. Kelly, T. S. B.: Non-Parasitic Extradural Cyst of the Spinal Canal, Lancet **2**:13-16, 1937.

14. Robertson, J. F., and Graham, C. P.: Spinal Extradural Cyst Associated with Kyphosis Dorsalis Juvenilis, Ann. Surg. **110**:285-290, 1939.

15. (*a*) Mayfield and Grantham.[7] (*b*) Mayfield and Spurling.[12] (*c*) Meredith, J. M.: Unusual Tumor and Tumor-Like Lesions of the Spinal Canal and Its Contents with Special Reference to Pitfalls in Diagnosis, Virginia M. Monthly **67**:675-687, 1940.

be observed. Typically, the cyst is composed of avascular fibrous tissue, and in most instances epithelial cells or their remnants line the inner surface. In the case reported by Adelstein,[4] however, the lining cells were absent. Cloward and Bucy [2] noted the resemblance of the lining cells to the cells of the arachnoid membrane.

Of the various explanations offered for the association of the condition known as kyphosis dorsalis juvenilis and the extradural cyst, that of Cloward and Bucy [2] appears to have the best anatomic and physiologic foundation. It has been repeatedly pointed out that the changes in the vertebrae are not of an inflammatory nature and do not predominantly or selectively involve the vertebral epiphyses. The term vertebral epiphysitis for the changes observed in the vertebrae is, therefore, not correct. These authors pointed out that in the loose areolar tissue of the epidural space there are many vascular channels, including the main venous drainage of the vertebral body. Drainage is by way of the large posterior central vein, which leaves the body of the vertebra at the center of its posterior surface, to be eventually drained by the intervertebral veins. This large central vein, which is joined by the anterior transverse and anterior longitudinal venous sinuses before emptying into the azygos system by the intercostal veins, is actually occluded by the pressure of the cyst, which is wedged between the bony wall of the canal and the dura mater. The changes in the vertebral bodies can, then, be explained on the basis of venous congestion and stasis within the body of the vertebra itself. The partial collapse of the contiguous vertebral bodies results in the rounded and fixed deformity, which is said to be self limiting and never severe, assuming an arrested state within a few months of the onset.

The improvement in the neurologic signs following removal of spinal fluid can be explained by the relaxation of tension in the cyst with lessened compression of the cord after removal of fluid from the cyst itself. It is probable that some relaxation of tension in the cyst also occurs through lengthening due to release of fluid from the subarachnoid space below the lesion, but the cyst wall appears to be relatively inelastic, and this factor is probably not a considerable one. Such a period of relief is likely to be followed within a relatively short time by returning signs of compression, due to replacement of the fluid removed from the cyst. This was demonstrated by the manner in which the cyst refilled with fluid after aspiration at the time of operation in the case described here. As has been emphasized by Cloward and Bucy,[2] it must be remembered that even in instances of complete obstruction of the subarachnoid space manometric rise on jugular compression may occur as a result of transmission of pressure, owing to the fluid content and cystic character of the tumor mass. Such transmission of pressure through a fluid-containing tumor of

the spinal canal has also been noted in certain vascular tumors. In such instances the presence of changes in the interpedicular spaces or myelographic studies will demonstrate the level, and in case of the latter, the presence, of a subarachnoid block.

Further light on the character of the fluid contained in the cyst and on the presence of free communication between the spinal subarachnoid space and the cyst may be had from a comparison of the chemical constituents of the fluid removed separately from the two spaces at the time of operation. Reference to table 2 indicates the

TABLE 2.—*Comparison of Spinal Fluid and Cystic Fluid Removed at Operation*

	Spinal Fluid	Cystic Fluid
Total nitrogen, mg./100 cc.	316.0	319.0
Potassium, mg./100 cc.	11.1	13.1
Calcium, mg./100 cc.	5.8	5.8

presence of similar or identical amounts of potassuim, calcium and total nitrogen in the two fluids. The difference in the amount of potassium is explained by the contamination of the fluid from the cyst with a very small amount of blood at the time of removal.

SUMMARY

1. A case of extradural spinal cyst associated with early roentgenologic manifestations of kyphosis dorsalis juvenilis and erosion of the pedicles is reported.

2. A possible diagnostic aid, consisting of clinical improvement following removal of spinal fluid with subsequent recurrence of compression of the cord, is presented.

3. Further clinical and anatomic evidence of the origin of the cyst as a herniation of the pia-arachnoid through the dura is given.

4. Chemical studies showing the similar or identical character of the fluid in the cyst and in the subarachnoid space are presented.

226 North Phelps Street.

Case Reports

PSYCHONEUROTIC REACTION TO MULTIPLE PSYCHOSES AMONG SIBLINGS

FRED FELDMAN, M.D.*
Instructor in the Department of Neurology and Psychiatry, Albany Medical College
NEW YORK

THE CONCURRENCE of mental illness in two or more members of the same family has long posed a problem of concern to psychiatry. In an older era, this problem was investigated almost exclusively from the point of view of the psychoses. Studies of heredity and of folie à deux best exemplify this older vantage point. More recently, the intrafamily conflicts giving birth to the psychoneuroses have emerged into the sunlight of objective inquiry. Psychoses and psychoneuroses have rarely been considered together, however. This paper reports a family of which at least 4, and perhaps 6, members were psychotic and stresses the effect of this knowledge in causing a psychoneurosis in another sibling, a soldier. The relation of psychoses and psychoneuroses is discussed from the standpoint of nomenclature, traditions and basic conceptions.

REPORT OF A CASE

A soldier aged 28 was admitted to the psychiatric division of a convalescent hospital in April 1946, complaining of headaches and easy fatigability. The family history was notable in that the paternal grandmother died in a psychiatric hospital. The diagnosis was probably senile dementia, since the patient remembered that she had first been hospitalized in her eighties. A paternal uncle was also mentally ill for many years, was hospitalized several times and was described by the patient as "very wild—he was always escaping from institutions." The mother and father were described as nervous but otherwise well; apparently, the father, a shipyard worker, was able to maintain the family at a marginal or somewhat better economic level. The patient stated that his father had always seemed more antagonistic toward him than toward the other children, and he recalled a dramatic incident when he was 10 or 12 in which he knocked his father down and out. He described his father as a steady worker, but "a man whose temper seems to dominate him. I think he's a sick man, too." The relationship to the mother, a somewhat passive woman, was apparently not close. The parents were frequently in conflict, but never to the point of separation. The patient recalled frequent quarrels in the home and much protecting of the children on the part of the mother against the temper tantrums of the father. On the whole, he remembered the home as one in which some degree of affection was manifested by both parents toward all the children during their formative years.

The patient had 11 siblings, 5 brothers and 6 sisters. Three sisters and 1 brother had been hospitalized with verified diagnoses of schizophrenia. One pair of twin sisters were hospitalized within six months of each other, at the age of 19; they were interned for a period of six months, in 1 case, and of twelve months,

* Formerly Captain Medical Corps, Army of the United States.

in the other, and had been released within the year prior to the patient's hospitalization. The patient stated that so far as he knew their adjustment was adequate except that one of the twins "talks all the time." The third of the schizophrenic sisters was first hospitalized at the age of 28, for one year; at the time of my interview with the patient she was 34 and living with her husband, but the patient said that "she doesn't sound right to me." The fourth schizophrenic sibling, a brother, was hospitalized at the age of 28 for about one year, had recently been discharged and was unemployed. Among the other 5 siblings were twin brothers, about whom the patient knew little except that they were both hospitalized at the age of 7. He expressed the opinion that one of the twins was never sick but was hospitalized only "because it was impossible for the family to take care of him." He was released at the age of 10 and subsequently made a fair adjustment. The other twin was still institutionalized, but the patient could not recall where and did not know the cause. Mental deficiency may perhaps be considered.

The patient was born and raised in New York city; he described himself in childhood as "nervous and easily upset." He was frequently truant from school, although attending "adjustment classes" until the age of 16. He was considered delinquent during adolescence and was twice arrested, once for forgery of a government check and once for stealing 28 cents out of a cash register. A suspended sentence was obtained on each occasion. After leaving school, however, he began to work and showed an increasingly better vocational adjustment, leaving a job only to improve himself and eventually earning about $50 a week as helper to a truck driver. He enjoyed the work chiefly because he was successful at it. He was married at 21, to a girl of 19, whom he described as a "good housewife and manager," and there followed a period of compatible emotional and sexual adjustment, during which 2 children were born.

The patient came into psychiatric channels while overseas, through the recommendation of the War Department, acting on the basis of a letter sent by the patient's mother. The latter wrote she had noted that the few times that she saw him "he was very much depressed and was unhappy." She indicated that the patient had always "worried a great deal" about the siblings who had been ill and that at the time of his induction he was ashamed to reveal the family history to the draft board. His feelings about induction had been mixed, since he desired to prove his capacities to himself and yet was reluctant to leave his wife and children. He was in service for several months in this country, adjusting satisfactorily, and was transferred overseas late in 1945. At the time he was first called in by the psychiatrist, he indicated that he had been aware of increasing tension since going overseas. His sleep was restless and broken by disturbing dreams. He vomited frequently, noted dizzy spells, found it difficult to concentrate and felt that his memory was impaired. Symptoms of this nature had never troubled him before, nor had he ever previously been aware of periods of depression, which now became frequent. The psychiatrist felt that the degree of anxiety and depression was sufficient to warrant hospitalization and evacuation to the United States.

On admission to the convalescent hospital in this country, the patient's status seemed somewhat improved. He related well to the therapeutist and displayed considerable insight. Although he reiterated the surface symptoms already itemized, he said spontaneously, "It's really my worry about what happened to all my brothers and sisters." He had always been concerned about the possibility of illness suddenly appearing in himself, and after the birth of his children his apprehension mounted. His fears were nourished by the anxiety of his wife, who began

to brood over the foredoom which threatened her children. The patient had on many occasions found it necessary to reassure her on grounds where he did not stand too firmly himself. The unbridgeable absence from her while he was overseas heightened his uncertainties about himself, his children and his wife's devotion. He was still mildly depressed and gave evidence of a passive, dependent, insecure personality, but nevertheless showed good achievement drive. Psychotherapy was carried on for three weeks at the level of reassurance and ventilation, with some interpretation concerning problems of inheritance of mental illness. On discharge, he was considerably improved and was urged to seek further psychiatric contacts for himself and his wife in civilian life.

Instances of four or more psychotic members in one sibship are so infrequently encountered that reports in the literature are still seen only semioccasionally. A survey of the literature of the past ten years revealed less than a score of recorded cases, most of them chronicled as examples of folie à deux, and several others illustrating the inheritance of mental illness. In only two papers are psychoneuroses mentioned, and in those only briefly and tangentially. Grover (1937), in a study of folie à deux, suggested that schizophrenic reactions and hysteria are related, since either may be precipitated by suggestion, although the delusions of hysteria are surrendered more easily than those of schizophrenia. Osborn (1945) reported on 5 psychotic sisters and noted the fact that several relatives asked questions concerning heredity, pointing out the physician's responsibility to be careful "not to scare the questioner half way to a psychosis . . . or to ignore the predisposition of these people to crack under life's stresses."

As compared with the psychoneuroses, the more dramatic, more circumscribed, more tangible psychoses adapted themselves easily to recording and statistical tabulations. Moreover, the coexistence of several cases of psychosis within the family group was relatively uncommon and therefore drew the scrutiny of investigators. In a more recent era, the psychoneuroses have come into focus as major problems, and the intrafamily conflicts so long hidden from view have been carefully examined.

A considerable gap has existed between these two large areas, that of the psychoses and that of the psychoneuroses—separated from one another by history, nomenclature, difference in methods of psychiatric training and discrepant levels of dynamic understanding. The bridges across this gap have increased at every point, until psychiatrists have arrived at broad, encompassing concepts of human behavior which make use of the older nomenclature for practical purposes only, while maintaining awareness of its inadequacies. Practical necessity still tends, in many instances, to segregate therapeutists into one group or the other. Most research projects are pragmatically limited by the same boundaries of surface symptomatology. Nevertheless, principles central to all the "functional" mental and emotional illnesses are being elucidated.

The problems of heredity, for example, have been explored carefully with reference to schizophrenia and the affective psychoses. Studies of mental illness appearing in several generations of one family have contributed to knowledge in this regard. Myerson studied a large series of cases illustrating the "horizontal" transmission of mental disease, reporting 2 instances involving 4 siblings and 1 involving 5 siblings. A closely related problem, which has been fairly widely examined, is that of the psychoses of association, or folie à deux. A recent exhaustive study of the literature by Gralnick (1942) yielded 103 cases of "communicated" psychoses, most of them involving 2 persons, but in 7 instances implicating 4 or more patients. In the numerous papers on folie à deux and multiple psychoses which have been reported, little reference has been made to the emotional impact of knowledge of the presence of the psychoses in the family on the normal members. Fear of inheritance of mental illness is, of course, widely discussed and easily understandable. In group therapy sessions conducted with psychoneurotic soldiers, for example, this problem was frequently brought up and insecurities and apprehensions of every degree on this score were laid open. Every psychiatrist has had to instruct and reassure relatives on this question innumerable times. The anxiety arising from the mental illness, especially a psychosis, of only one close relative may be considerable. When derangement seems to strike one's siblings one after another, misgivings about one's own future are appreciable.

The case described is certainly not an unusual one so far as it concerns the reaction of the patient to a threat, possibly greater than he could control. His insecurity is patent, and stands as one blade in a forest of insecurities of present day society. The special note comes from the presence of an unusual degree of severe mental illness in his kinship, constituting the menace to him. The steps from his feeling of vulnerability to the anxiety depression can be traced more precisely, in terms of his basic dependent personality, his undirected strivings for achievement, the significance of his successful marriage and, finally, the mounting precariousness of his position away from his family. Once the situation was changed, the relatively simple reaction subsided.

This case has been reported because it offers another small opportunity to break away from the shackles of a nomenclature which separates all mental illnesses into two large groups and tends to keep them divided. Had this patient been more deeply depressed, his illness might have been labeled a psychosis, and thus, through the vagaries of nomenclature, a "record" for mental illness in one sibship might have been built up. Sufficient data concerning the siblings are, unfortunately, not available in this case to analyze differentially the factors of association, heredity and intrafamily conflict.

SUMMARY AND CONCLUSION

The case of a soldier reacting psychoneurotically to the appearance of psychoses in 4 brothers and sisters is described. The reaction is readily understood, but is of additional interest in that it serves to draw attention to the chasm which divides the psychoses from the psychoneuroses. This gap has historical origins, is perpetuated by nomenclature and is, indeed, a practical necessity. Research and observation, however, may take cognizance of additional relationships between the two large groups of mental illness and may point to a future when more dynamic concepts will underlie nomenclature.

275 Central Park West.

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FIBRILLARY (PILOCYTIC) ASTROCYTOMA IN THE FLOOR OF THE FOURTH VENTRICLE

DWIGHT PARKINSON, M.D.
ROCHESTER, MINN.

ALTHOUGH Bailey [1] stated that astrocytomas may occur anywhere within the brain, the paucity of reported cases in the literature leaves the general impression that they do not arise from the floor of the fourth ventricle. None is so indicated in the most comprehensive reviews in the English literature [2] of the past fifteen years. A case of fibrillary astrocytoma of the floor of the fourth ventricle is therefore presented.

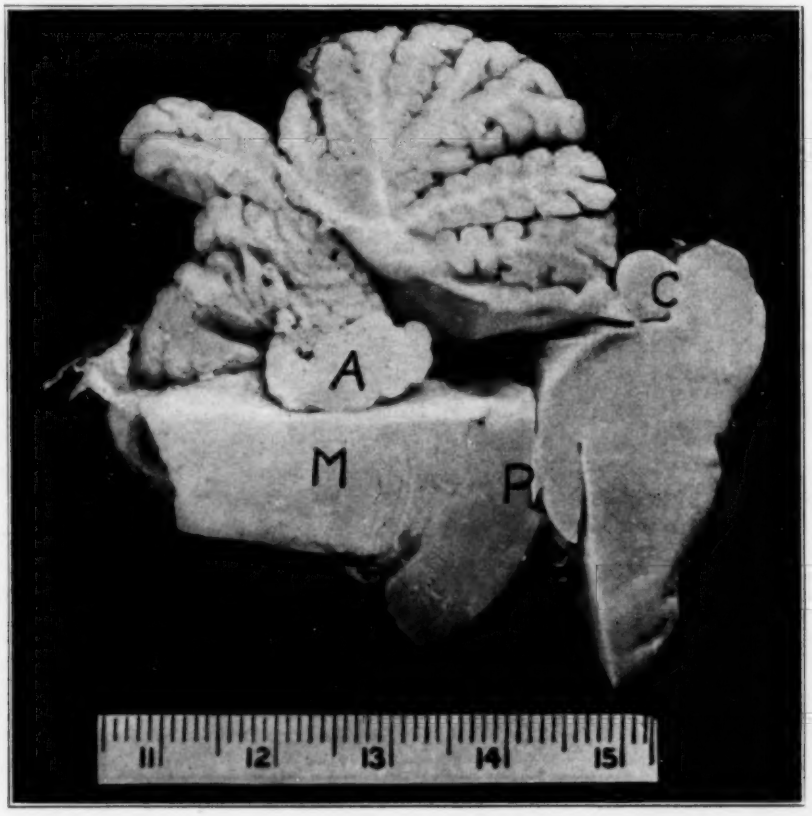

Fig. 1.—The astrocytoma (*A*) as it rests on the floor of the medulla (*M*), completely free in the cavity of the fourth ventricle except for the narrow attachment to the floor. The pons (*P*) was inadvertently sectioned before the tumor was noted. *C* indicates the corpora quadrigemina.

From the Department of Pathology, Dartmouth Medical School, and the Mary Hitchcock Memorial Hospital, Hanover, N. H.

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(Footnotes continued on p. 609)

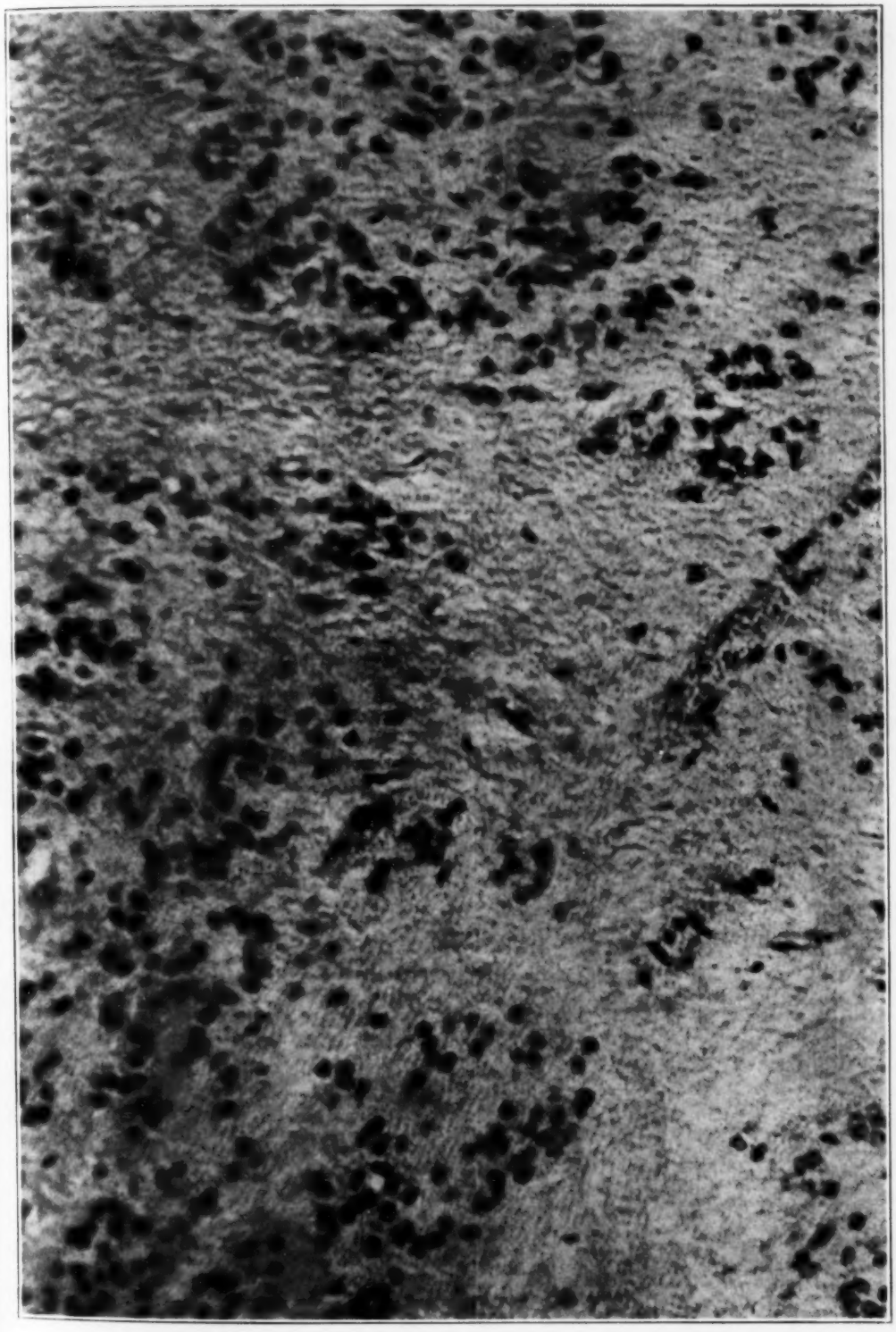

Fig. 2.—Microscopic section from the central portion. Phosphotungstic acid hematoxylin stain; × 40.

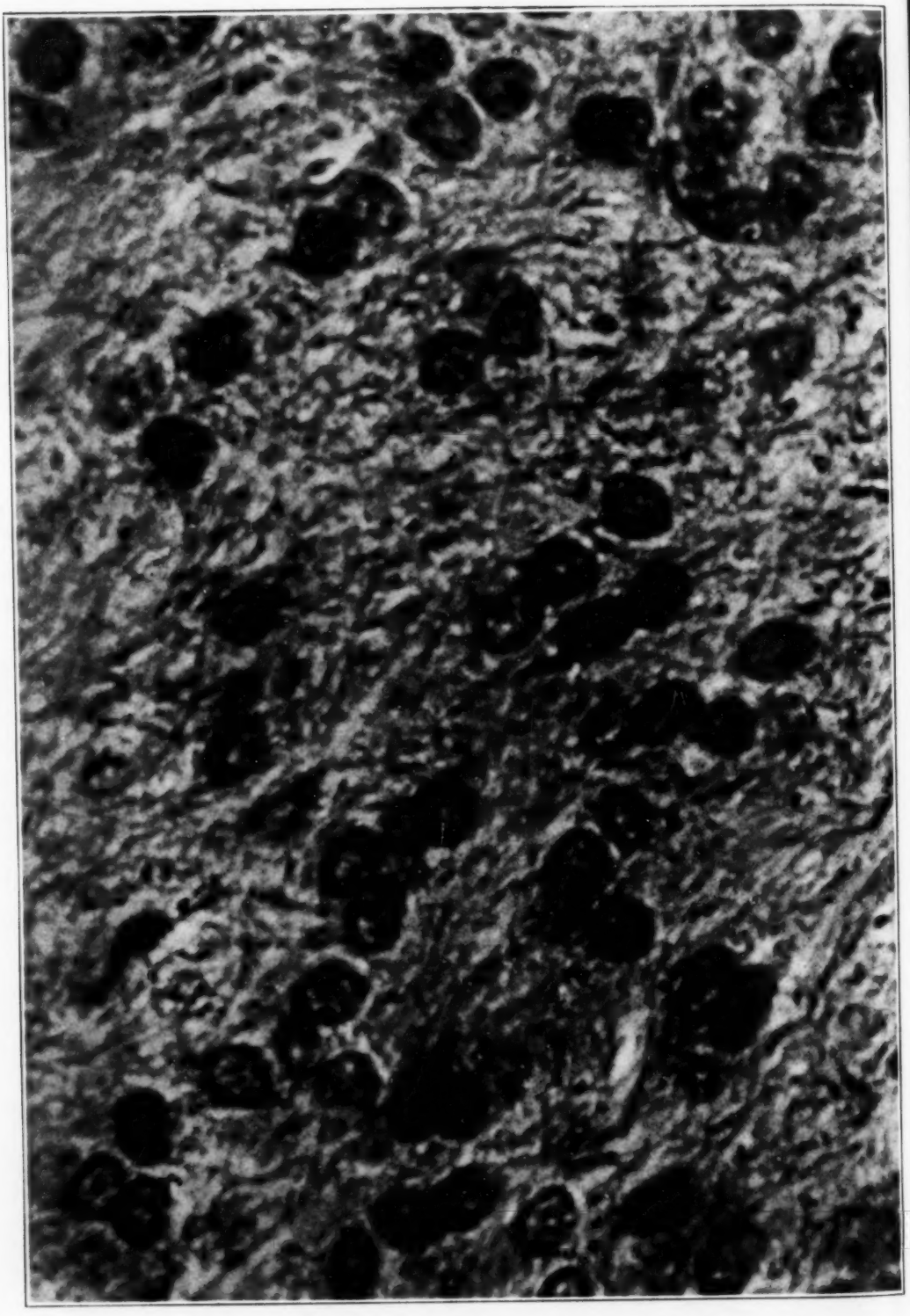

Fig. 3.—A portion of the field shown in figure 2; × 176.

REPORT OF A CASE

H. B., a white woman aged 50, was admitted to the hospital with signs and symptoms of intestinal obstruction. Exploratory laparotomy revealed inoperable ovarian carcinomatosis with bilateral ovarian dermoid cysts. Death followed four days later as a result of pulmonary embolus.

At no time in her history or hospital course was there any evidence of intracranial tumor.

Routine examination of the brain revealed a firm, nodular, gray-white tumor, measuring 1.8 by 1.4 by 1.4 cm., in the fourth ventricle. It arose by a stalk 0.1 cm. in diameter from a point 0.5 cm. anterior to the obex and 0.2 cm. to the right of the midline (fig. 1). It had elevated the tela choroidea in the portion immediately over the tumor. There was no apparent interference with the outflow of cerebrospinal fluid at the foramen of Magendi, and there was no dilatation of the ventricular system. The sectioned surface was glistening gray-white, with no evidence of cyst formation.

Microscopically, with the hematoxylin and eosin stain, irregular clusters of vesicular nuclei were seen which appeared devoid of surrounding cytoplasm. Between these was a loose feltwork of eosinophilic strands, constituting the great bulk of the tumor and containing numerous small vessels. At the periphery the strands assumed a more orderly tangential arrangement.

With a phosphotungstic acid hematoxylin stain the nuclei and chromatin granules were dark blue with strands of the feltwork light blue (figs. 2 and 3). Some of these strands could be seen to terminate in dark blue expansions on the walls of vessels, which in contrast stained yellow-brown.

With the Gomeri silver method the nuclei, feltwork and capillary walls stained gray-brown and the larger vessel walls gray-pink.

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Special Article

REHABILITATION OF THE PARAPLEGIC PATIENT

COMMANDER EDWARD W. LOWMAN (MC), U.S.N.

OF ALL war casualties, the hope of none has received a greater boost than that of the paraplegic patient. What was once blank invalidism is now self sufficiency and independence. No longer need the paraplegic patient be an economic liability, a charge on society, sapped of self respect and initiative, confronted only by an empty horizon. His is a new perspective, a broader horizon, crystallized in the rehabilitation accomplishments of the recent war.

The attainments and advancements of the war were doubtless primarily the consequence of the large number of cases of traumatic transverse myelitis, which posed so urgent a problem that it became necessary to establish centers (nineteen in the Army, one in the Navy) for the specialized treatment of these injuries. The segregation thus in large numbers afforded the opportunity, the facilities and the personnel for mass observation, evaluation and standardization of treatment procedures. In one Navy hospital, 63 such patients comprised a group on which these observations are based.

The rehabilitation of the paraplegic patient is a joint undertaking, requiring the closest cooperation of the urologist, the neurologist and the physiatrist. The observations and advances of the first two have been adequately presented elsewhere.[1] It is the purpose here to discuss

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

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the role of the physiatrist and the proper application of his specialty, physical medicine (which comprises physical therapy, occupational therapy and physical reconditioning), to the problem.

The ultimate objective of physical medicine in the care of the paraplegic patient is self-sufficient reambulation. The steps in the attainment of this definitive result, briefly, are:

1. Maintenance of normal joint range for the prevention or correction of contracture deformities.

2. Development through resistive exercises of maximum power in remaining normally innervated muscle groups for use in reambulation.

3. Mobilization and utilization of all residual functional muscle tissue in partially denervated groups through serial muscle test evaluations, muscle reeducation and remedial exercises.

4. Prophylaxis against and treatment of decubitus ulcers.

5. Application of and instruction in use of reambulation devices for accomplishment of independent reambulation and normal personal care.

6. Encouragement of economic rehabilitation.

7. Maximum utilization of occupational therapy for functional, diversional and/or vocational objectives.

NORMAL JOINT RANGE

The maintenance of normal joint range is an imperative prerequisite to satisfactory reambulation.

The severe spasticity frequently encountered in the paraplegic patient and the prolonged disuse of joints secondary to the paralysis or to muscular weakness are both factors conducive to muscle shortening, which, in turn, is the precursor to contracture and contracture deformity. The cycle of spasm—muscle shortening—contracture deformity should be constantly borne in mind. The degree of reversibility of the cycle through physical medicine is in inverse ratio to the time lapse prior to institution of such measures. Treatment, therefore, must be instituted early.

From the start, each patient must be taught good bed posture in order to minimize postural deformities. Beds should be equipped with bedboards; and, when spasticity permits, the use of footboards for the prevention of mechanical foot drop should be insisted on.

In the presence of spasticity, heat (for its relaxing effect) is applied to the patient in bed for fifteen to thirty minutes once or twice daily, in accordance with the degree of pain. The involved joints, then, are carried to the extent of tolerance through a normal range of motion

with gradual, steady forcing to overcome the resistance offered by the spasticity. Massage for the spastic patient is generally poorly tolerated; this, however, is a general rule, and not infrequently light sedative massage will be well tolerated and will aid in providing greater relaxation of spasticity.

For the patient who can be transported by stretcher without aggravation of his spasticity (and most fall into this category), treatment can best be carried out in a Hubbard-Currance tank bath, the optimum water temperature being 98 to 102 F. (fig. 1). The effect of massage

Fig. 1.—Hydrotherapy in a Hubbard tank should be prescribed early for the paraplegic patient.

provided by the underwater air ejectors may or may not, as in the case of manual massage, be well tolerated. Sessions in the tank are carried out daily for periods of thirty minutes each. Forcing of joints through normal ranges of motion and stretching of shortened muscles can be effected under water with much greater efficiency and less discomfort to the patient than at the bedside.

In the case of the flaccid patient, deep, sedative massage is employed routinely in conjunction with the procedures previously described for the maintenance of good circulation and nutrition of the skin and the prevention of orthostatic rubor, coldness and swelling.

As the patient acquires automaticity of bladder control and regularity of bowels, either voluntarily or by enemas, he is admitted to the

therapeutic pool. This pool is indoors; is heated at a constant temperature of 92 F.; is shallow, with a maximum depth of 66 inches (167 cm.), and is equipped with underwater plinths and walking bars. In the pool the patient receives further daily stretching (fig. 2), remedial exercises and muscle reeducation and graduates to standing and walking with the aid of the bars.

PHYSICAL RECONDITIONING

Physical reconditioning for the development of maximum power in unaffected muscle groups should be started immediately after the acute phase of the illness. Since efficient reambulation will be dependent

Fig. 2.—Restoration of shortened muscles to normal length and muscle reeducation can best be effected in a heated pool.

directly on the strength of remaining innervated muscle groups, so will it be expedited by maximum development of these groups. Bed exercises must be prescribed and carried out once, twice or many times daily, depending on the tolerance of the patient. At first they may consist of mild calisthenic procedures, such as breathing exercises, neck rolling, active arm and shoulder movements and abdominal tensing. They must be graduated progressively to resistive exercises. Each bed should be equipped with an overhead swinging ("monkey") bar. Resistive spring devices for arm, chest, shoulder and hand exercises are good agents to provide resistance for the bed patient.

Once the patient is out of bed, the regimen of exercises becomes more rigorous. In addition to his swimming exercise in the heated pool, he reports daily to the gymnasium and there begins mat exercises—exercises for the lower and the upper part of the back, push-ups, sit-ups, etc. Thus, building arm, shoulder and torso strength, he begins to utilize this strength in graduated doses, in lifting himself, ape fashion, with his arms from place to place around the mat, from mat to stool and then to higher stools, from stool to wheel chair and back, from wheel chair to toilet, from wheel chair to bath tub, from wheel chair to bed, etc. Progressively, he acquires increasing strength and self reliance.

MUSCLE REEDUCATION AND REMEDIAL EXERCISE

It should be the constant goal to mobilize and utilize to the fullest all residual functioning muscle. It should be remembered that much of the initial disability associated with traumatic transverse myelitis may be, and often is, a physiologic lesion, the result of edema, hemorrhage and compression of the cord, which may resolve quickly or persist until decompression by the neurosurgeon. This apparent partial reversibility has led neurosurgeons more and more to abandon conservative tendencies and to make surgical exploration early. Repeated muscle tests and persistent muscle reeducation must be carried out by the physiatrist or the physical therapist in order to maintain a valid evaluation and to effect best results.

In the case of weak muscles with partial residual innervation graduated strengthening exercises must be initiated, so that maximum function through hypertrophy of remaining intact muscle units may be obtained. In cases of very weak muscles, these exercises may at the start be electrically induced with apparatus, preferably painless galvanic-condenser machines. Underwater exercises, active or passive, with elimination of gravity, constitute the next step, and so on, to a level of resistive gymnasium procedures, depending on the potential capacity of the remaining intact muscle units. The latter must be prescribed, supervised procedures carried out with the aid and direction of the physical therapist.

DECUBITUS ULCERS

Decubitus ulcers are a constant hazard in the paraplegic patient and often occur despite the best nursing precautions. Bony areas with thin protective paddings of tissue are most predisposed to the production of pressure disruption of blood flow and consequent ulceration; common sites of predilection are over the sacrum, the femoral trochanters, the iliac crests and the heels. The best treatment is a vigilant prophylaxis—frequent changing of position (at least every two hours), use of rubber protective rings, prevention of friction burns from sheets, maintenance

of dry bedclothes, daily baths and daily massage of predisposed pressure areas. A common precipitant to be avoided is the trauma from careless shifting of the patient between stretcher and bed, inducing friction bruises.

Ulcerations are not a contraindication to Hubbard baths, but, on the contrary, are stimulated to more rapid healing by the heat of the water and by the massage effect of the underwater air ejectors. Daily local applications of ultraviolet radiation after this hydrotherapy is of therapeutic benefit in stimulating epithelization. The ultraviolet radiation is sometimes best applied with an applicator in order to reach undermined and sloughing deep areas.

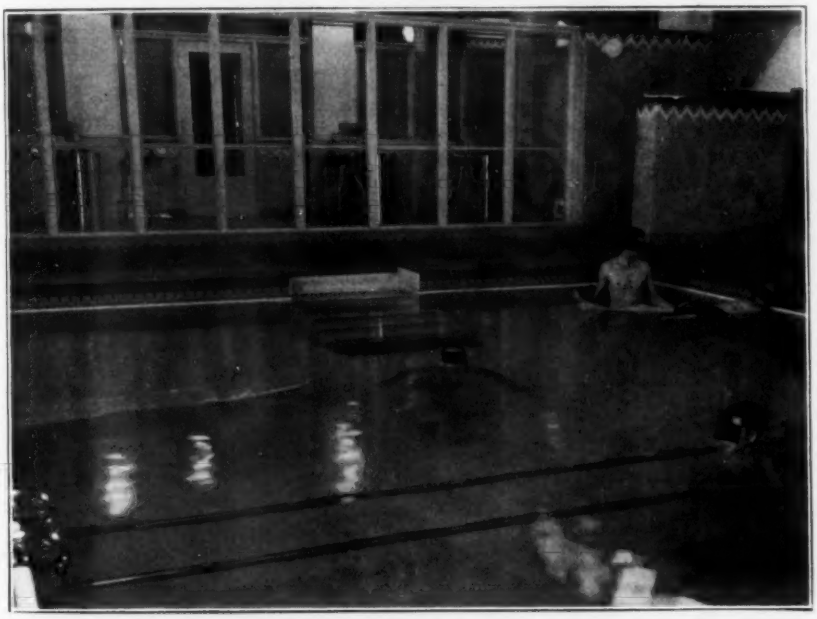

Fig. 3.—Vertical standing in a pool is the first stage in reambulation.

REAMBULATION

The vertical stance is best started with walking bars in the therapeutic pool (fig. 3). This renews the patient's acquaintance with upright posture and is a stimulus to his personal confidence, which will be needed for the mastery of reambulation on crutches and braces. For the patient with only partial paraplegia, stand-balance exercises, postural training, pelvic stabilization and weight shifting may be carried out for weeks or months in the pool before sufficient strength is attained to permit accomplishment of such feats against gravity.

Braces should be prescribed as soon as residual spasticity is sufficiently mild to permit their application. At best, braces are a crude mechanism and a poor substitute for normal means of body support

and locomotion. Each rehabilitee is in himself an individual problem and requires individualized evaluation before decision is reached on the type of bracing to be tried. Braces are locomotive aids, and, as such, augment means for ambulation; they should be built as a supplement to the patient's residual muscle power, and not as a substitute. Bracing should, therefore, be minimal within the bounds of necessity for the individual patient; this is particularly important in any case in which any degree of further return of functional strength is in the offing. Too

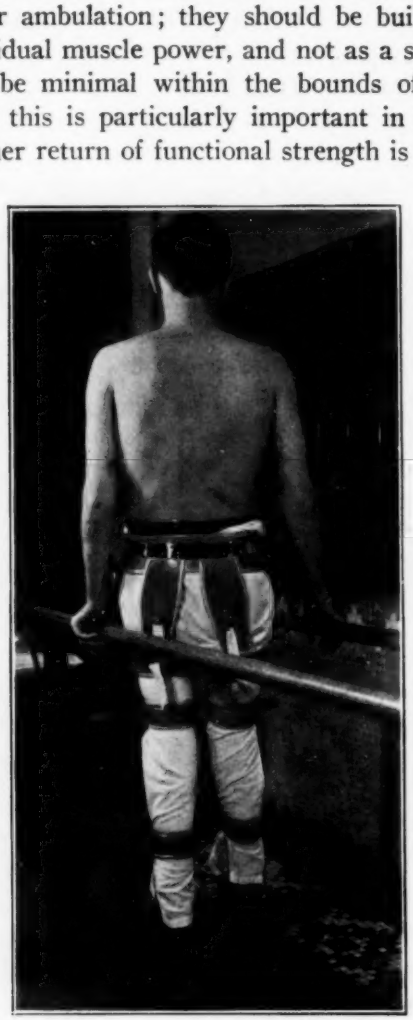

Fig. 4.—The stand-balance exercise and weight shifting are carried out in parallel bars with braces.

extensive bracing in such cases provides superfluous immobilization and thus removes the demand for work which is the cause of hypertrophy of the residual intact muscle units.

It is a great help to have the services of a well experienced brace maker, whose qualifications include not only technical skill and ingenuity but also a knowledge and appreciation of functional anatomy and body mechanics. The patient with a weak quadriceps musc'e, for example, obviously presents a different problem from the patient with a paralyzed

quadriceps and should not be fitted with a long leg type of brace. Similarly, the patient with a weak anterior tibial muscle and normal peroneus muscles presents a different problem from the patient with peroneal palsy and requires different bracing. The cripple with loss of both the gluteal and the abdominal muscles requires considerably greater mechanical support than the patient with innervated abdominal muscles. Yet, too often bracing is standardized in broad types.

The decision for specific bracing depends on the individual picture presented by the patient's muscle test. Modifications in conformity with

Fig. 5.—Mastery of obstacles is imperative for maximum self sufficiency.

further need for support or with improvement in muscular power are to be expected and met. Not infrequently a patient may start with long leg braces and subsequently graduate to dropped-foot braces as the result of return of or increase in power in muscle groups.

Once braced, the patient must start the tedious and prolonged task of learning to utilize his residual muscle power in the manner most efficient for ambulation. First comes the stand-balance exercise, repeated day after day in parallel bars (fig. 4), at the foot of a bed or in a mechani-

cal walker. This mastered, he then must learn weight shifting from leg to leg to maintain balance. Finally comes the first step. In all of these procedures, the patient is putting to use the increased strength attained in the preceding weeks and months of bed and gymnasium reconditioning exercises. In learning walking, he relies at first on parallel bars, later on a mechanical walker and ultimately on crutches.

The type of crutch gait selected for the individual patient depends on the extent of his paralysis. With complete involvement of both lower extremities, the gluteal muscles and the abdominal muscles, a swing-through type of gait is the maximum accomplishment. As the degree of involvement decreases, the type of and need for crutch gaits, canes or braces vary accordingly.

With his aids to reambulation, the patient must be taught proper use for his maximum self sufficiency (fig. 5). He must master such ordinarily simple obstacles as stairs, inclines, curbs, toilets, automobiles, beds and chairs. He must be required before release to have attained at least an average dexterity in a standardized list of such feats of accomplishment. The subject of crutch walking and mastery of obstacles has been well covered in the writings of Deaver.[2]

ECONOMIC REHABILITATION

The sponsorship and encouragement of vocational training during the prolonged period of rehabilitation of the paraplegic patient are of the utmost importance. The pursuit of economic readjustment while he is still a patient provides not only sound preparation for return to society but is potent prophylaxis against inanition, introspection and the morbidity that often is bred of the idleness of prolonged convalescence. This is a medical problem which cannot be shifted elsewhere, but must be demanded and guided as such. The present hospital vocational training program in Veterans Administration hospitals for paraplegic patients is an admirable acceptance of this expanded concept of medical responsibility.

OCCUPATIONAL THERAPY

Occupational therapy fulfils a threefold function for the paraplegic patient. When functional results are desired, such as the correction of a deformity or the strengthening of a specific muscle group, the use of appropriate crafts or skills is to be carried out on prescription and under the direction of a trained occupational therapist. This, however, applies to only a limited group of patients. For all patients, diversional or

2. Deaver, G. G., and Brown, M. E.: Challenge of Crutches: Methods of Crutch Management, Arch. Phys. Med. **26**:397-403 (July) 1945; Challenge of Crutches: Crutch Walking, Muscular Demands and Preparation, ibid. **26**:515-525 (Aug.) 1945; Challenge of Crutches: Standard Crutch Gaits and How to Teach Them, ibid. **26**:573-582 (Sept.) 1945.

avocational arts and skills should be provided by occupational therapy. Such work may be carried out both in wards for the bed patient and in shops for the patient who is up and about. In this diversional work, the valuable aid of volunteer skilled civilian groups, such as the Red Cross Arts and Skills Corps, should be generously utilized. When, for certain patients, arts and skills may prove of vocational benefit, occupational therapy dovetails into and coordinates its work with the vocational training program.

MORALE

The maintenance of high morale in the paraplegic patient is dependent on (1) good medical and nursing care, (2) honesty with the patient and (3) the prevention of hospital fatigue through the maximum utilization of the patient's idle time in pursuits of a diversional, avocational or vocational nature. While verbally easy to analyze, this maintenance of morale is in many respects the most difficult actually to achieve, and, at the same time, the most important objective, for on its attainment largely rests the success of the entire program of both physical and mental rehabilitation.

SUMMARY

The successful rehabilitation of the paraplegic patient in wartime military hospitals has opened a new vista of hope for the "hopeless" cripple.

The rehabilitation of the paraplegic patient is the joint responsibility of the urologist, the neurologist and the physiatrist.

The objectives of physical medicine in the program are sevenfold: (*a*) maintenance of normal joint range for the prevention or correction of contracture deformities; (*b*) development of maximum muscle power in the remaining innervated muscle groups for use in ultimate reambulation; (*c*) use of muscle testing, muscle reeducation and remedial exercises for salvaging the maximum function from the damaged muscle units; (*d*) prophylaxis against and treatment of decubitus ulcers; (*e*) application of and instruction in use of reambulation devices; (*f*) encouragement of economic rehabilitation, and (*g*) maximum utilization of occupational therapy for functional, diversional and/or vocational objectives.

2030 Fairburn Street, Los Angeles (25).

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

TERMINAL DEGENERATION WITHIN THE CENTRAL NERVOUS SYSTEM AS STUDIED BY A NEW SILVER METHOD. P. GLEES, J. Neuropath. & Exper. Neurol. **5**:54 (Jan.) 1946.

Glees describes a silver method which gives excellent results with both frozen and pyroxylin sections, staining the nerve fibers in their terminal arborizations, both in the normal state and in the process of degeneration. With the latter it is necessary, first, to determine the appropriate time at which the degenerative process becomes histologically visible. This varies with the age and species and with the different parts of the central nervous system.

The silver method reported differs from the Bielschowsky method in two main respects: A different concentration of silver nitrate is employed, and preliminary treatment of the sections with the ammonia-alcohol solution (6 drops of ammonia in 50 cc. of alcohol) is introduced. This procedure dissolves the greater part of the myelin and thus provides the basis for a much more evenly stained section. Other advantages of the method are the perfect staining of the myelinated and non-myelinated fibers and the light brown color of the nerve cells. The staining of the nerve cells allows the more intimate study of the relation between the surrounding nerve fibers and the nerve cell protoplasm.

The term "terminal degeneration" is used to cover the degeneration of the terminals of the *bouton* type and the free nerve ending. The *bouton* type of degeneration within the spinal cord is on the whole very conspicuous, owing to the abundance of terminal rings in the normal state. This view has been arrived at not only by means of the technic reported here, but by other variations of the silver impregnation methods. Even with careful examination of the normal cerebral cortex, it is difficult to demonstrate ringlike endings. The synapse within the cortex is mainly represented by free terminals of the pericellular plexus.

GUTTMAN, Philadelphia.

DEVELOPMENT OF THE HUMAN LATERAL GENICULATE BODY. E. R. A. COOPER, Brain **68**:222, 1945.

Cooper, in a study of human embryos, observed that the lateral geniculate body derives its pars dorsalis from the lateral thalamic nucleus and that the pars ventralis is subthalamic in origin. The pars dorsalis is recognizable at the 22 mm. stage, at the time when the optic tract reaches this region of the thalamus. The pars dorsalis is the first nuclear mass to be differentiated in the thalamic portion of the diencephalon. The pars ventralis appears at the 35 mm. stage. Lamination of the lateral geniculate body does not appear until the sixth month of fetal life, and from the onset of lamination there are six U-shaped and V-shaped laminas, with their closed convex aspects placed laterally and ventrally. The optic tracts enter the ventrolateral convexities, and the optic radiations emit from the dorsomedial concavities. The four outermost and larger laminas are comprised of small neurons, while the two smaller and innermost laminas are made up of large neurons. Cooper disproves the previously held opinion of eversion of the laminas

in the human or the monkey lateral geniculate bodies, for the curvature in lemurs and in higher primates is always in the same direction and the convexity always receives the optic tract.

FORSTER, Philadelphia.

Physiology and Biochemistry

BLOOD OXYGEN SATURATIONS AND DURATION OF CONSCIOUSNESS IN ANOXIA AT HIGH ALTITUDES. CARL E. HOFFMAN, ROBERT T. CLARK JR. and E. B. BROWN JR., Am. J. Physiol. **145**:685 (March) 1946.

Hoffman, Clark and Brown observed subjects at simulated altitudes of 28,000 to 38,000 feet (8,500 to 11,000 meters) and studied (1) the periods of useful consciousness, (2) times to the appearance of tremor and imminent unconsciousness and (3) oxygen saturations of the blood at termination of useful consciousness, at appearance of tremor and at imminent unconsciousness. The times of imminent unconsciousness varied from one hundred and forty-one seconds, at 28,000 feet, to forty-seven seconds, at 38,000 feet. The time of useful consciousness was approximately three-fourths the time that consciousness was retained. Oxygen saturations of the blood averaged 64 per cent at the appearance of the first error and 56 per cent at the time of imminent unconsciousness.

FORSTER, Philadelphia.

INACTIVATION OF POLIOMYELITIS VIRUS BY "FREE" CHLORINE. G. M. RIDENOUR and R. S. INGOLS, Am. J. Pub. Health **36**:639 (June) 1946.

Newer knowledge on chlorine testing has made it possible to measure more accurately the concentration of free or uncombined chlorine in the hypochlorous state in organically polluted solutions. This is done by the orthotolidine-arsenite test. The test gives a measurement of the "free chlorine"; the combined chlorine, such as the chloramines, or the total available chlorine. In contrast to previous studies, this investigation showed that chlorine is an effective inactivating agent for the Lansing strain of poliomyelitis virus if related to the actual "free," or uncombined, chlorine residual in solution. The amount of "free" chlorine needed for inactivation is well within the range of doses used in water treatment and swimming pool sanitation when the "break point" method of chlorination is employed.

J. A. M. A.

RADIOTHERAPY AND INTRACRANIAL PRESSURE. MARIA BORISOVNA TSUKER, Am. Rev. Soviet Med. **2**:316 (April) 1945.

Tsuker reports her observations on the effect of roentgen therapy on the cerebrospinal fluid. Data are presented on a group of 19 adult dogs who were subjected to small doses of roentgen radiation. The following factors were constant for all experiments: current, 160 kilovolts and 4 milliamperes; filter, 0.5 mm. of copper and 1.0 mm. of aluminum; field, 13 by 18 cm.; target skin distance, 30 cm. Each treatment dose was 160 r, repeated three or four times, with a total dose of 480 to 640 r, or from three-fourths to one erythema dose. The vertex was the only field treated, and treatments were given at intervals of several days.

Spinal fluid was obtained through suboccipital puncture, performed one or more times. The initial pressure was compared with the pressure after the treatment provided there were no great fluctuations due to extraneous factors, such as fear. Determinations of the pressure were made on 13 dogs after exposure and were repeated several times, at various intervals, on 8 of the dogs. Sixty-five experiments on 13 dogs, before and after roentgen therapy, were analyzed.

The suboccipital puncture was always made under morphine anesthesia. The pressure was measured with a water manometer, which consisted of a U-shaped graduated glass tube filled with a weak solution of potassium permanganate and connected by a rubber tube with one outlet of a three way stopcock. The needle was attached by tubing to another of the outlets, while the third remained free and served as the control. Readings of absolute pressure registered on the manometer may not correspond to those on more sensitive standard manometers. Only the comparative pressure, and not its height before and after the treatment, was considered. Furthermore, fluctuations obtained with a more sensitive apparatus would be much wider than those obtained in the experiments. Measurements obtained on restless animals were discarded. Insufficient observation and infrequent readings are probable reasons for the discrepancies noted in various reports. It is necessary to make repeated determinations at various intervals after exposure.

The data indicate that, under the conditions described, intracranial pressure is lowered after roentgen irradiation. The decrease in pressure appeared immediately in about one-half the animals and became more pronounced later. Observations were terminated after six weeks, so that no conclusion on the duration and constancy of the lowered pressure is available.

In another series of experiments, on 6 dogs, the effect of roentgen radiation on the absorption of cerebrospinal fluid was determined. In these experiments, atropine sulfate and pilocarpine hydrochloride were introduced into the cerebrospinal fluid by suboccipital puncture. The times required for pupillary dilation and salivation were measured.

Analysis of the data shows that immediately after roentgen irradiation there was a considerable increase in the speed of absorption, but that the rate was not constant. In a few days to two weeks the increased absorption was followed by delayed absorption. The rate of absorption was further observed four to six weeks later in 4 dogs, in 2 of which it was studied twice. In 3 of the 4 dogs the rate approximated that before treatment, and in 1 dog the rate was considerably decreased after six weeks.

The rate of absorption varied at different intervals after roentgen therapy. Immediately after treatment absorption was accelerated, and during the next three to fourteen days it was delayed. This delay was more pronounced than the preceding acceleration but was variable as compared with the initial speed of absorption prior to roentgen treatment. The rate of absorption approached the original value after four to six weeks, and at times dropped below it.

The rapid increase in the rate of absorption may be explained by the effect of roentgen rays on blood vessels, producing hyperemia. Since the changes are physiologic rather than structural, the result of the action of roentgen rays on absorption is not constant.

Histologic studies were made on 10 dogs (9 adults and 1 puppy) subjected to roentgen radiation. Controls were prepared from 2 adult dogs and 1 puppy. Fibrosis was observed in the vascular network of all 10 dogs, with patchy areas in the stroma and subepithelial areas. In the 2 adult controls, but not in the control puppy, areas of fibrosis also appeared. In the puppy treated with roentgen rays, fibrosis was prominent. It is well known that vascular fibrosis in man may result from infections and intoxication. The development of fibrosis of the cerebral vessels in treated dogs may be due to repeated injections of morphine before the experiment and to the toxic effects of ether-chloroform anesthesia.

In the vascular fields of all dogs treated with roentgen rays, but not in the controls, deeply stained, shrunken epithelial cells were observed. The histologic

data correspond with those obtained by Schafer, Sgalitzer, Spiegel and others, who also noted pyknotic epithelial cells in the cerebral vascular networks after roentgen therapy of the skull.

In addition, cells with finely granular, pale-staining cytoplasm and large vesicular nuclei were seen. Some cells were smaller and vacuolated, with irregular margins. The controls had many more epithelial cells in stages of active secretion than had dogs treated with roentgen radiation. The cerebral vascular networks of dogs treated repeatedly with roentgen rays contained shrunken epithelial cells and only a few epithelial cells in an active secretory phase.

The effect of roentgen rays on intracranial pressure may be interpreted as follows: The lowered pressure of cerebrospinal fluid seen a few days after treatment is the result of accelerated absorption, and the lowered pressure seen two to six weeks later is the result of diminished secretion of cerebrospinal fluid, due to impaired function of the epithelium.

Tsuker states that these data may explain many contradictory clinical observations. Roentgen therapy is effective only in cases of hydrocephalus in which elevated intracranial pressure is caused by increased production or delayed absorption of cerebrospinal fluid or, frequently, by a combination of the two factors. In cases of hydrocephalus produced by mechanical obstruction of the cerebrospinal circulation, roentgen therapy is valueless. Favorable results in cases of communicating hydrocephalus were obtained, especially the acute form. Roentgen irradiation failed to relieve obstructive hydrocephalus. Roentgen therapy is most effective in cases of acute increase of pressure. With chronic hydrocephalus it is less satisfactory unless treatment is repeated frequently. Roentgen therapy is of value also in cases of injuries to the skull with increased intracranial pressure.

GUTTMAN, Philadelphia.

DISTRIBUTION OF INTRAVENOUSLY INJECTED FRUCTOSE AND GLUCOSE BETWEEN BLOOD AND BRAIN. J. R. KLEIN, R. HURWITZ and N. S. OLSEN, J. Biol. Chem. **164**:509, 1946.

Fructose (levulose) injected intravenously, in contrast to dextrose (*d*-glucose), does not maintain the electrical activity of brain or relieve symptoms of hypoglycemia in eviscerated animals. However, the rate of respiration of brain slices in the presence of fructose does not differ significantly from the rate in the presence of dextrose and the oxidation of fructose by broken cell preparations of brain follows the same pattern as that for dextrose. A hypothesis which would explain these findings is that the rate of transfer of fructose from blood to brain in vivo is not sufficient to provide a concentration of sugar that would meet the metabolic requirements of the brain. In the present work, the distribution of fructose and glucose between the arterial blood plasma and the cerebral hemispheres of cats was determined at various times after intravenous injection of these sugars. They are such as to indicate that the rate of transfer of fructose from blood to brain is considerably less than that of glucose. The concentrations of fructose found in brain were less than the concentrations of glucose required to maintain normal central function of the nervous system.

PAGE, Cleveland.

OBSERVATIONS ON THE MECHANISM OF ELECTRICALLY INDUCED CONVULSIONS. F. REITMAN and B. W. RICHARDS, J. Nerv. & Ment. Dis. **102**:421 (Oct.) 1945.

In order to test the significance of cerebral vasoconstriction associated with induced convulsions, a group of 16 patients receiving electroshock therapy were given intravenous injections of a preparation of nicotinic acid ("pelonin") in doses

of 50 to 100 mg. just before the application of a strength of current previously sufficient to cause convulsions. In 61 per cent of the patients the development of convulsions was inhibited by the drug. When amyl nitrite was given by inhalation to the same patients, convulsions were prevented in 59 per cent.

The authors believe that these results indicate that cerebral vasoconstriction is one of the basic mechanisms involved in electrically induced convulsions.

CHODOFF, Washington, D. C.

DORSAL ROOT POTENTIALS OF THE SPINAL CORD. J. C. ECCLES and J. L. MALCOLM, J. Neurophysiol. **9**:139 (May) 1946.

Eccles and Malcolm studied the dorsal root potentials set up in the frog's spinal cord by either dorsal or ventral root volleys. The authors confirmed previously reported experiments and obtained additional information. The dorsal root potential was found to be a catalectrotonic potential propagated electrotonically from a central focus and analyzable into an active, initial phase and a later phase of passive decay. Dorsal root potentials set up by strong or repetitive stimuli of the dorsal roots were found to have in addition a prolonged phase due to internuncial after-discharge, this phase being increased by convulsant drugs, such as strychnine, curarine and veratrine, whereas it was diminished by a narcotic, such as pentobarbital. Pentobarbital sodium was found to prolong greatly the time constant of delay but to have no effect on the rising phase. The dorsal root potential recorded in a dorsal root was found to be abolished during the spike of a maximum volley fired in through that root, and to recover in part during the decline of the spike. The dorsal root reflex which is often associated with the dorsal root potential conforms in all respects to the hypothesis that the impulses are fired by the cathodal polarization of the central terminals of these fibers. Eccles and Malcolm describe the mechanism of a reversed electrical transmission across the synapse.

FORSTER, Philadelphia.

A MIDBRAIN MECHANISM FOR FACIO-VOCAL ACTIVITY. A. H. KELLY, L. E. BEATON and H. W. MAGOUN, J. Neurophysiol. **9**:181 (May) 1946.

Kelly, Beaton and Magoun observed before operation the potentialities of cats for faciovocal expression and then produced bilateral lesions in the diencephalon or midbrain. Lesions of the hypothalamus at the level of the mamillary bodies, interrupting all known descending hypothalamic connections; interruption of the afferent paths to the thalamus; rostral lesions of the midbrain, and tectumectomy each failed to alter the faciovocal activity of the cats. Central lesions in the midbrain destroying the periaqueductal gray matter and adjacent tegmentum beneath the superior colliculus abolished or greatly reduced the faciovocal activity. Stimulation of this region elicits faciovocal behaviour. Kelly, Beaton and Magoun conclude that there is a central midbrain mechanism for integrating faciovocal behavior in emotional expression.

FORSTER, Philadelphia.

BRAIN STEM FACILITATION OF CORTICAL MOTOR RESPONSES. R. RHINES and H. W. MAGOUN, J. Neurophysiol. **9**:219 (May) 1946.

Rhines and Magoun observed the effects of exploratory stimulation of the brain stem on motor activity induced reflexly and by stimulation of the motor cortex in cats and monkeys. The authors found that cortically induced movements were facilitated by stimulating a mechanism in the ventral portion of the diencephalon which appears to receive functional contributions from the globus pallidus

and the nuclei of the midline and other thalamic nuclei. An uninterrupted continuity of facilitatory sites may be followed from the ventral portion of the diencephalon through the central gray matter and the tegmentum of the midbrain, the pontile tegmentum and the reticular formation of the medulla. Sites in the ventral part of the diencephalon stimulation of which facilitates cortically induced movements also facilitate motor activity evoked from the bulbar pyramid, even after cortical extirpation. Therefore the facilitation due to diencephalic stimulation is mediated within the spinal cord. Impairment of this facilitatory system in the brain stem may be responsible for the hypokinesia which follows experimental destruction of the globus pallidus and the ventral portion of the diencephalon.

FORSTER, Philadelphia.

TRANSMISSION OF IMPULSES IN PERIPHERAL NERVES TREATED WITH DI-ISOPROPYL FLUORPHOSPHATE ("DFP"). FREDERICK CRESCITELLI, GEORGE B. KOELLE and ALFRED GILMAN, J. Neurophysiol. **9**:241 (May) 1946.

Crescitelli, Koelle and Gilman employed diisopropyl fluorophosphate in studies on the role of acetylcholine in the transmission of nerve impulses. Diisopropyl fluorophosphate has an irreversible anticholinesterase action. The experiments included in vivo and in vitro exposure of sciatic nerves to the drug, with subsequent study of conduction in the nerves. The authors found that local application of physostigmine or diisopropyl fluorophosphate in Ringer's solution to segments of isolated nerves led to block of impulses, indicated by failure to record action potentials in the nerve beyond the region of application. The block of impulses was not irreversible, for washing the exposed segment in Ringer's solution or merely removing it from the solution of diisopropyl fluorophosphate abolished the effect.

In vivo administration of diisopropyl fluorophosphate to bull frogs produced a reduction in the cholinesterase content of the nerves to a mean value of 2.3 per cent of that in control nerves. This indicated to the authors that the experimental nerves had virtually no acetylcholine-splitting activity. However, such nerves conducted impulses as well as control nerves.

Crescitelli, Koelle and Gilman conclude that there is no relation between the magnitude of the spike potential and the cholinesterase activity of the nerve fibers and indicate that the block produced by diisopropyl fluorophosphate was not due to anticholinesterase activity.

FORSTER, Philadelphia.

TREATMENT OF EXPERIMENTAL LIVER CIRRHOSIS. JAMES V. LOWRY, Quart. J. Stud. on Alcohol **6**:271 (Dec.) 1945.

Albino rats at weaning were placed on a deficient diet (no. 545). They received 20 per cent ethyl alcohol as their sole source of fluid. A cirrhosis-like reaction of the liver was observed histologically in biopsy material which was removed sixty-three to eighty-four days after the rats were subjected to this regimen.

One group of the surviving animals continued to receive the same diet with the addition of 40 mg. of choline chloride daily; the other group received a similar diet and an increase in the casein content. All were given water for seven days after the biopsy. Then, some of these rats were placed on the alcohol regimen, but a few continued to receive the water. This treatment was continued for some animals up to a year.

The livers of the rats treated with choline chloride showed decided improvement in the gross and microscopic appearance. There was a lesser, but definite, improvement in the livers of the animals who had received an increase in casein. Although

therapy had no recognizable effect on the fibrous tissue present, it apparently prevented further progression of the cirrhosis and produced a notable improvement in the histologic appearance of the parenchyma.

BECK, Buffalo.

ALCOHOL AS A PREVENTIVE OF EXPERIMENTAL NEUROSES. JULES H. MASSERMAN, Quart. J. Stud. on Alcohol **6**:281 (Dec.) 1945.

Ten cats were trained in successive stages to perform activities whereby the behavior patterns of each animal could be observed and graded according to a standard scale. The animals had to be induced to partake of alcoholic solutions, as normal cats refuse to drink them. After the behavior pattern of each animal was adequately determined under the influence of various doses of alcohol, the animal was subjected to shock stimuli that induced severe conflicts in the feeding situation. Only 3 of the animals exhibited a relatively mild neurosis when they had received 2 to 2.5 cc. of alcohol per kilogram of body weight.

When the conflicts were again induced in these 3 animals without ingestion of alcohol, they became severely neurotic. Five of the others, who had not shown emotional instability, also manifested strong neurotic behavior.

Masserman concludes that alcohol affords partial protection against the neurotogenic effects of conflictual experiences. This might be the result of one of the following mechanisms: diminution in the acuity of sensory experiences; disorganization of perceptual-integrative response formations, or impairment of retention of such reaction patterns as are temporarily formed. An attempt to correlate these observations with parallel phenomena in human behavior was made. Human beings have learned to drink alcoholic beverages either to cloud, and thereby mitigate, anticipated stresses, or as a hypnotic to blunt and disorganize neurotic anxieties.

BECK, Buffalo.

TRANSIENT DISTURBANCES FOLLOWING GUNSHOT WOUNDS OF THE HEAD. W. RITCHIE RUSSELL, Brain **68**:81, 1945.

Russell points out that head injury from a blunt object produces instantaneous and widespread arrest of cerebral activity with relatively little focal injury, whereas injuries from missiles of high velocity produce predominantly focal signs, frequently without loss of consciousness. Wounds which present surgically no more than penetration of the scalp may overlie an area of cerebral bruising, with concomitant clinical signs. With small, superficial injuries of the brain the immediate effect indicates that the cortex has been rendered inert. Thus, injuries to the midrolandic area produce paralysis and numbness of the opposite upper extremity—the phenomenon of corticospinal shock. In the transient symptomatology sensory and motor components cannot be separated. With injuries to the motor region the lower extremity recovers from the shock state faster than does the upper extremity. The nearer the injury to the rolandic area, the severer is the transient sensory-motor disturbance and the greater the likelihood of permanent sequelae. The distribution of sensory loss after wounding tends to include the entire extremity. This effect is compared to the intra-areal firing by strychninization described by Dusser de Barenne. Deep pressure pain recovers quickly after rolandic wounds; cutaneous sensibility recovers slowly and incompletely. The remaining hypalgesia may be patchy and so slight as to be considered due only to cortical lesions. The induction of hypalgesia by cortical lesions is contrary to Head's concept that cortical injuries cannot alter the threshold for primary types of cutaneous sensation. The cortex of area 3 is buried within the rolandic fissure, and study of

penetrating lesions in this area reveals that they are associated with hypalgesia. However, permanent loss of all forms of sensation results only from limited wounds of the rolandic area, while gross injuries to the same area permanently destroy discriminative sensory functions only. This paradoxic situation is as yet unexplained. Hyperpathia, similar to the so-called thalamic syndrome, may occur with lesions of the postcentral gyrus.

FORSTER, Philadelphia.

A STUDY OF PUPILLARY INEQUALITIES IN MAN. ERIC A. TURNER, Brain **68**:98, 1945.

Turner describes the use of cocaine and epinephrine drops in elucidating the underlying cause of pupillary inequality in clinical cases. The test was employed in 50 control cases and in 66 cases of pupillary inequality. The results suggest that the commonest cause of pupillary inequality in cases of head injury is partial paresis of the third nerve, in which pupillary changes may occur without external ophthalmoplegia. In cases of intracranial aneurysm Horner's syndrome of long standing may dilate but little and become irregular in outline.

FORSTER, Philadelphia.

INTRATHECAL PENICILLIN THERAPY: IMMEDIATE REACTIONS IN THE SPINAL FLUID. J. M. TAQUES BITTENCOURT, Arq. de neuro-psiquiat. **4**:65 (March) 1946.

Taques Bittencourt reports on changes in the spinal fluid in 16 patients given intrathecal injections of penicillin. Fifteen patients had parenchymatous neurosyphilis, and 1, osteitis syphilitica with a normal spinal fluid. Prior to intrathecal therapy, the neurosyphilitic patients showed pleocytosis, with a count as high as 150 cells per cubic millimeter and a median count of 8 cells. In most cases the cells were lymphocytes. In 2 cases the cells increased to 600 per cubic millimeter, after treatment, and in 2 cases there were over 1,000 per cubic millimeter. The percentage of polymorphonuclear leukocytes increased as the cells became more numerous. Toward the end of the intrathecal therapy the spinal fluid became yellow, due partly to the penicillin and partly to the red cells in the fluid. In the case of osteitis syphilitica the cells increased to 152 per cubic millimeter, with 100 per cent lymphocytes. In all cases there was an increase in protein proportionate to the pleocytosis. The usual increase in protein was 5 to 10 mg. per hundred cubic centimeters. A greater increase was noted in 3 cases: In 1 case, with 100 cells per cubic millimeter in the spinal fluid after treatment, there was an increase in protein of 30 mg. per hundred cubic centimeters; in the second case, with 250 cells (72 per cent polymorphonuclear leukocytes), there was an increase of 60 mg., and in the third case, an increase of 190 mg., with no evidence of manometric block. There was no increase in protein in the case of syphilitic osteitis. The colloidal gold curve showed little modification. In a few cases the curve tended to become of mixed type. The Wassermann and Steinfeld reactions became more positive, for the hematoencephalic barrier permitted the more ready passage of antigens from the blood.

N. SAVITSKY, New York.

RELEASE OF PHOSPHORUS FROM ELECTRICALLY EXCITED BRAIN. VICENTE H. CICARDO, Pub. d. Centro de invest. tisiol. **9**:115 (June) 1945.

The brains of 50 dogs, anesthetized with sodium pentobarbital, were stimulated electrically by means of an induction current. Specimens of blood were examined for phosphorus before and after electrical stimulation. In order to exclude the role

of muscular contractions, blood from the superior longitudinal sinus was compared with blood from the femoral artery and vein. Electrical stimulation was continued from two to five minutes. The method of Fiske and Subbarow was used to determine the phosphorus in the blood. A definite increase, up to 31 per cent, in the amount of phosphorus in the blood was noted after cerebral excitation by the electric current. After a rest of fifteen minutes the values often returned to normal. Repetition of the excitation sometimes caused an even greater amount of phosphorus to be liberated into the blood. The amount of phosphorus in the blood taken from the superior longitudinal sinus was always higher than that from the femoral artery or vein. In order more completely to exclude the role of muscular contractions, similar studies were made after section of the spinal cord just below the bulb. The same increase in phosphorus in the venous sinus was found after this procedure. The liberation of phosphorus was also not impeded by curarization of the animals. In the curarized animals, however, a second series of excitations after a rest of fifteen minutes did not result in as great an increase in the amount of phosphorus in the blood; the results were inconstant, and not very definite. In general, the amount of phosphorus obtained in curarized animals, even after the first series of excitations, was less than in the other animals. The author believes that curare impedes the liberation of phosphorus into the blood as the result of some central action.

N. Savitsky, New York.

Neuropathology

Central Nervous System in Pneumonia (Nonsuppurative Pneumonic Encephalitis): II. Pathologic Study. H. H. Noran and A. B. Baker, Am. J. Path. **22**:579 (May) 1946.

Noran and Baker collected brain from 10 cases of pneumonic encephalitis in which complete necropsies were performed. In all instances evidence of encephalitis was established by microscopic study. The cerebral alterations were uniform throughout the entire series, even though the cause of the pneumonitis was highly variable. Extensive thrombosis and prominent perivascular hemorrhages were the principal microscopic lesions in the nervous system. The prodigious number of thrombosed cerebral vessels suggests that some alteration in the clotting mechanism of the blood may cause these cerebral lesions. The constancy of the cerebral lesions, regardless of the type of pneumonia, indicates that the real cause of encephalitis may be the pulmonary tissue itself. Some factor from the parenchyma of the lung may possibly accelerate intravascular clotting.

J. A. M. A.

Degeneration of the Basal Ganglia in Monkeys from Chronic Carbon Disulfide Poisoning. Richard Richter, J. Neuropath. & Exper. Neurol. **4**:324 (Oct.) 1945.

Four monkeys (Macaca mulatta) served as subjects in this investigation. The animals were exposed daily, five days a week, to carbon disulfide vapor for approximately six hours each day over a period of twenty to twenty-one months. On several occasions acute intoxication, of an accidental nature, occurred. After death, complete serial pyroxylin sections through the cerebral hemispheres and through the cerebellum and brain stem of each animal were prepared. These were stained routinely with cresyl violet and by the Smith and Quigley method for myelin. Sections including the lesions were also prepared with the hematoxylin-eosin-azure stain, the Van Gieson method, the Holzer stain, and the Perdrau and Davenport methods of silver impregnation. Representative levels from the spinal cord were examined. Sections of parts of the brachial plexus and the sciatic nerves

from the thigh were stained with hematoxylin and eosin, with stains for myelin sheaths and by the Bodian silver method for axis-cylinders.

In all the animals the essential and pathologic changes consisted in extensive bilateral and symmetric necrosis of the globus pallidus and the zona reticulata of the substantia nigra. The monkeys presented in common profound motor disturbances characterized by reduction and slowness of all types of movement without pareses, absence of coordination in locomotion and climbing, plastic cogwheel rigidity of the skeletal muscles, flexor postural attitudes of the trunk and extremities and severe action and tension tremor. Richter states that the data justify the conclusion that the motor syndrome observed in the animals is attributable to destruction of the globus pallidus and substantia nigra and that there are close similarities pathologically and physiologically to the parkinsonian syndrome of man.

GUTTMAN, Philadelphia.

KORSAKOFF'S PSYCHOSIS: REPORT OF A CASE. M. REMY, Monatschr. f. Psychiat. u. Neurol. **106**:128, 1942.

Remy reports a typical case of Korsakoff's psychosis of ten years' duration which had an alcoholic basis. The anatomic changes were limited entirely to the mamillary bodies. In Remy's opinion, this case supports the conclusion that the mental disturbances characteristic of Korsakoff's psychosis are due to the cutting off of nerve impulses which normally travel along the tractus mamillothalamicus to the thalamus and thence to the cerebral cortex.

ROTHSCHILD, Worcester, Mass.

Meninges and Blood Vessels

ELECTROENCEPHALOGRAM IN SUBARACHNOID HEMORRHAGE. LOUIS GREENSTEIN and HANS STRAUSS, J. Mt. Sinai Hosp. **13**:76 (July-Aug.) 1946.

Greenstein and Strauss studied 29 cases of subarachnoid hemorrhage according to a method previously described by Strauss (*J. Mt. Sinai Hosp.* **9**:1-19, 1942). A definite correlation was found to exist between clinical cortical foci and focal abnormalities in the electroencephalogram. An electroencephalographic focus was found in 7 cases, in only 1 of which focal signs were absent on clinical examination. The electroencephalographic focus in this exceptional case was no longer present when a second recording was made, two weeks later. In 18 of the 29 cases only a meningeal syndrome was presented. Of these 18 cases, the electroencephalographic record was normal in 6, and showed a low degree of diffuse abnormality in 9, a high degree of diffuse abnormality in 2 and a high degree of abnormality with a focus in 1. Of the 6 normal records, 1 was obtained on the third day and 1 on the sixth day, with blood in the spinal fluid. Neither the finding of blood in the spinal fluid nor the presence of meningeal signs bore any relation to the electroencephalographic picture. In all cases the degree of abnormality in the electroencephalogram showed progressive diminution on repeated examinations at intervals of increasing length. No increase in the degree of electroencephalographic abnormality was noted in subsequent records once the hemorrhage had ceased. The authors believe that cortical changes due to the presence of blood cannot be postulated as the main cause of electroencephalographic abnormalities in cases of subarachnoid hemorrhage. They postulate that the diffuse electroencephalographic abnormalities may be due to a dysfunction of the deep centers close to the third ventricle. The deep centers may be easily affected in cases of subarachnoid hemorrhage, since many such hemorrhages arise from vessels at the base of the brain. The authors also point out the importance in differential diagnosis of

repeated electroencephalographic records. The diminution of electrocortical activity is against the diagnosis of a bleeding tumor and in favor of a subarachnoid hemorrhage due to some other cause.

N. SAVITSKY, New York.

Diseases of the Brain

ANALYSIS OF BRAIN ABSCESSES OBSERVED DURING THIRTY YEARS. E. SACHS, Ann. Surg. **123**:785 (May) 1946.

Sachs says that during the past thirty years 142 cases of cerebral abscess have been observed at his clinic. In 128 of these cases the abscess was encountered at operation. In 12 of the remaining 14 cases in which the abscess was not located the patients were treated before the discovery of ventriculography. That the mortality at his clinic was higher than at other clinics he ascribes partly to the fact that he operated on every patient with an abscess of the brain, regardless of the seriousness of the patient's condition. He believes that an unencapsulated abscess should not be drained. During the acute stage penicillin is invaluable in bringing about encapsulation. Aspiration, except in cases of cerebellar abscess, should be used only as a palliative procedure until more radical treatment can be instituted. Excision without drainage is the ideal procedure, but frequently marsupialization must be resorted to if, in the course of an excision, the abscess has been ruptured.

J. A. M. A.

INVOLVEMENT OF CENTRAL NERVOUS SYSTEM IN INFECTIOUS MONONUCLEOSIS: REPORT OF TWO CASES. J. DER. SLADE, New England J. Med. **234**:753 (June 6) 1946.

Slade cites 2 cases which illustrate the encephaloneuronitic and encephalomyelitic types of infectious mononucleosis. In both cases there was evidence of permanent damage to the nerve tissue. At the time of the patient's admission the clinical impression was that of infectious mononucleosis. When the paralytic symptoms appeared, poliomyelitis was considered; but the Paul Bunnell titer in cases of poliomyelitis is not higher than 1:28. Clinical observations support the concept of infectious mononucleosis as a generalized infection with localization in one or more of the tissues or organs of the body. In the cases described there was apparently diffuse and spotty involvement of the nervous system. The clinical picture is similar to that produced by viruses of other diseases and suggests that this, too, may be a virus infection. Infectious mononucleosis is a potentially serious disease.

J. A. M. A.

Peripheral and Cranial Nerves

NUTRITIONAL DISORDERS OF THE NERVOUS SYSTEM IN THE MIDDLE EAST. J. D. SPILLANE, Proc. Roy. Soc. Med. **39**:175 (Feb.) 1946.

Two types of nutritional polyneuritis were seen among Polish troops and refugees after two to four years in Russian internment camps, with resulting widespread malnutrition. In the largest group of patients the symptoms antedated examination by six to twelve months. Sharp pains in the soles and the muscles of the calf resulted in difficulty in walking similar to that of claudication. Coldness and paresthesias of the feet were distressing symptoms. Muscular tenderness and atrophy and weakness of the extensors of the toes and feet, with sensory loss and reflex disturbances, appeared subsequently. The symptoms of the second group were characterized by the rapid onset of paralysis, in direct relation to an acute infective, debilitating illness. In a few fatal cases the Wernicke syn-

drome was observed clinically and at autopsy, but occasionally hemorrhagic changes were seen in the brain stem at autopsy where none had been demonstrated clinically. Intramuscular injection of thiamine improved the appetite and the pains but did not influence the period of incapacity or hasten restoration of muscular power or reflex activity.

In another series, of over 200 repatriated internees and prisoners of war, 20 to 100 mg. of thiamine hydrochloride given daily for one or two weeks failed to produce demonstrable improvement over the status of patients who received no additional supplement of vitamins.

BERRY, Philadelphia.

NOCTURNAL CHEIROBRACHIALGIA PARAESTHETICA: SCALENUS SYNDROME; STUDY OF 70 PERSONAL OBSERVATIONS. R. FROMENT and WEGELIN, Presse méd. **54**: 282 (May 4) 1946.

Froment and Wegelin report 70 cases of nocturnal cheirobrachialgia paresthetica occurring in 62 female and 8 male patients between the ages of 7 and 74 years, among whom were 59 between the ages of 30 and 60 years. One third of the patients were definitely neuropathic. The syndrome occurred in the upper extremities of the patients during the night and consisted of paresthesia of the fingers and of the hand, associated with pains of the sympathetic type in two thirds of the patients. Seventeen patients presented mild edema of the upper extremities. The disorder was elicited by the immobilization of the extremities and disappeared after energetic mobilization of the extremity involved. Many patients showed a spontaneous tendency to improvement, but there were also patients whose condition was refractory. Satisfactory results were obtained in 18 cases from treatment with sedatives, barbituric acid derivatives, antispasmodics and, occasionally, sympathicolytic or vasoconstriction substances. This method of treatment was ineffective in 14 cases. Infiltration of the stellate ganglion was practiced in 8 cases, with satisfactory results in 2. The concept of sympathetic hyperexcitability supported by subclavicular venous stasis rather than that of a pathologic condition of the scalenus muscles is suggested for this condition.

J. A. M. A.

THIAMINE AND POLYNEURITIS DIPHTHERICA. K. WASSMANN, Acta med. Scandinav. **124**:27, 1946.

Wassmann treated 10 patients with postdiphtheritic paresis of the palate at the department of epidemic diseases of the Frederiksberg Hospital in Copenhagen. Five of the patients received one intramuscular injection of 20 mg. of thiamine hydrochloride in 2 cc. of distilled water, and the remaining 5 patients received 2 cc. of isotonic solution of sodium chloride daily for twelve to twenty days. The average duration of the paresis was twenty-six days in the vitamin-treated group and thirty days in the control group. There was therefore no convincing difference between the two groups. Paresis of the extremities was produced by injection of a mixture of diphtheria toxin and diphtheria antitoxin in 40 guinea pigs. Twenty animals were given intramuscular injections of large doses of thiamine hydrochloride, while the remaining 20 animals received no treatment. There was no pronounced difference between the vitamin-treated group and the control group with respect to frequency, severity or duration of the paresis or the time of its occurrence. Thiamine hydrochloride has no prophylactic or therapeutic effect on postdiphtheritic paresis in guinea pigs.

J. A. M. A.

Vegetative and Endocrine Systems

EXPERIMENTAL PITUITARY DIABETES OF FIVE YEARS' DURATION WITH GLOMERULOSCLEROSIS. F. D. W. LUKENS and F. C. DOHAN, Arch. Path. **41**:19 (Jan.) 1946.

Diabetes produced in a dog by injections of a pituitary extract was observed for five years and found to be of constant severity after the first year. Autopsy

revealed lesions resembling those which have previously been noted in cases of diabetes, viz., fatty deposits in the liver and the kidneys. In addition, intercapillary glomerulosclerosis, which has not hitherto been reported in association with experimental diabetes, was noted.

WINKELMAN, Philadelphia.

MATING BEHAVIOR IN MALE RATS CASTRATED AT VARIOUS AGES AND INJECTED WITH ANDROGEN. FRANK A. BEACH and A. MARIE HOLZ, J. Exper. Zool. **101**:91 (Feb.) 1946.

Castration of male rats at ages ranging from 1 to 350 days was followed by a period of several months, after which the responses of the castrated rats to receptive females were tested. The capacity for sexual arousal was distinctly limited in all the castrated animals. The mating activity which did occur showed no relation to the age at which castration was performed.

Although the administration of androgen resulted in the appearance of the copulatory reaction on the part of all castrated males, the response was less complete in the rats castrated on the day of birth. The differences in behavior are probably due directly to inhibition of development of the penis. Replacement therapy failed to compensate for the lack of testicular secretion during the critical period of penile growth (from birth to 21 days of age).

The overt behavior of males castrated at birth to androgen given during adult life indicates that the essential neuromuscular mechanisms are fully organized and normally sensitive to the testicular hormone. The high proportion of incomplete copulations and the failure of ejaculation are the result of absence of a well developed penis, and hence of an important source of sexual stimulation.

REID, Boston.

Cerebrospinal Fluid

UPPER LIMITS OF NORMAL PROTEIN CONTENT OF THE CEREBROSPINAL FLUID. V. KAFKA, Monatschr. f. Psychiat. u. Neurol. **110**:325, 1945.

Kafka examined 500 cisternal fluids and found that the upper limit of the total protein content is 1.1 graduation marks, as compared with 1.3 graduation marks for the lumbar fluid. These values are equivalent to approximately 26.4 mg. per hundred cubic centimeters for the cisternal fluid and 31.2 mg. per hundred cubic centimeters for the lumbar fluid if the graduation mark of the special tube is accepted as equivalent to 24 mg. per hundred cubic centimeters. Kafka designates his method of determination as "protein relation," it being his aim to relate the individual values and compare them for different diseases. This method of protein relation is suited to the determination of the upper limits of the total protein content. Various observations have indicated that for the determination of the protein relation it is essential not only to ascertain the centrifugation time and the number of revolutions but also to determine the protein content of a graduation mark. If this is done, great differences will not be detected between the results of the protein relation and the Kjeldahl determination. It is also pointed out that the various modifications of the Kjeldahl method involve certain sources of error. The author further mentions a serial method which is a simple control and directs attention to numerous minor manipulations that help to avoid errors.

J. A. M. A.

Special Senses

NATURE OF STARVATION AMBLYOPIA. A. R. HAZELTON, J. Roy. Army M. Corps **86**:171 (April) 1946.

Hazelton presents the results of a survey of patients complaining of dimness of vision among prisoners of war held by the Japanese in Thailand. The total number of patients examined was 277. The cause seemed to be bound up with a

combination of vitamin deficiencies. The disease resolved itself into two parts: 1. Easy exhaustion of the ciliary muscle, which was cured by the administration of thiamine hydrochloride, at least 1,000 international units intramuscularly per day for fourteen days. There were also the symptoms of eyestrain, i. e., pain in the eyeballs, frontal headaches, excessive lacrimation, heaviness of the lids and tired feeling of the eye, which increased after close work on reading and were alleviated by administration of thiamine. 2. A condition of degeneration of the cones of the retina, which was probably brought about by insufficient photosensitive substance for these receptors. The degeneration of the cones was shown by (*a*) lowering of the visual acuity, (*b*) inability to differentiate objects close together and (*c*) interference with color vision. The insufficient amount of photosensitive substance is postulated from the fact that the color of print changed on reading from black to green to yellow. Two facts emerge from this study: 1. There is a relation between eyestrain and thiamine deficiency. 2. Persons with avitophthalmia are liable to sustain further damage to their cones in bright light and so should not work in the sunlight and should wear dark spectacles. As the retina is of central nervous system origin, any degeneration of the organ is probably permanent; so the prognosis for these cases is bad. The results of treating patients with nutritional amblyopia of short duration with 10 eggs per day for thirty days were gratifying; all persons undergoing this treatment showed improvement, and 1 patient was cured.

J. A. M. A.

Encephalography, Ventriculography, Roentgenography

VALUE OF ROUTINE ROENTGENOGRAPHIC STUDIES OF WAR INJURIES OF THE HEAD AND NECK. GILBERT N. HAFFLY, Arch. Otolaryng. **41**:216 (March) 1945.

Haffly stresses the value of routine roentgenographic studies of all war injuries of the head and neck. He reports the case of an infantry officer who was struck in the left orbital region by a fragment of artillery shell. The left globe was enucleated, and a large ragged laceration of the left lower eyelid and adjacent region of the cheek was repaired with linen sutures within three hours after injury at a nearby evacuation hospital. Despite available roentgenographic facilities, no studies were considered necessary. Several days later, after he had been evacuated to the rear, routine roentgenographic studies revealed the presence of a comminuted fracture of the maxilla involving the inferior rim of the orbit. In addition, there was a large metallic fragment lying just below the left orbit close to the nares on the left side and within the cavity of the left maxillary sinus. The foreign body was disengaged with considerable difficulty and was found to be a fragment of an artillery shell, measuring 4 by 1.75 cm. Convalescence was uneventful.

RYAN, Philadelphia.

CEPHALHEMATOMA DEFORMANS: LATE DEVELOPMENTS OF INFANTILE CEPHALHEMATOMA. A. SCHÜLLER and F. MORGAN, Surgery **19**:651 (May) 1946.

A unilateral bulging of the anterior part of the skull was presented by a man and 4 women aged 20, 27, 54, 71 and 72, respectively. It was unusual for the patients to complain of symptoms referable to the cranial abnormality. Roentgenographic examination revealed an extensive hyperostosis as the basis of the deformity. Diploic hyperostosis prevailed in the calvaria and eburnated hyperostosis in the basal area. Osteoporosis and sclerotic islands; large, sequestrum-like fragments of bone, and sharply outlined cavities inside the diploe were characteristic features of the structure. Pneumatization was wanting or atypical in the hyperostotic area. The name cephalhematoma deformans seems adequate for this peculiar type of hyperostosis.

J. A. M. A.

Congenital Anomalies

ANALYSIS OF THE KLIPPEL-FEIL SYNDROME. C. A. ERSKINE, Arch. Path. **41**:269 (March) 1946.

In 1912 Klippel and Feil described the pathologic anatomy in a case of absence of the neck in a 46 year old man. The anatomic basis of the syndrome, since known by their names, consists essentially in congenital fusion and numerical reduction of the cervical vertebrae. Since the original description of this rare condition, most of the communications have been reports of clinical cases of a less extreme type. The three characteristic clinical features of the syndrome are shortness of the neck, limitation of movement of the head and lowering of the hair line.

From the case of the Klippel-Feil syndrome presented here, and from the cases reported in the literature, Erskine concludes that the essential features of the cervical deformity are synostosis of two or more cervical vertebrae and flattening and widening of the vertebral bodies. A numerical reduction of the vertebrae is an incidental, rather than an essential, part of the disorder, as is spina bifida. The latter depends largely on the degree of abnormality of the vertebral bodies. There is evidence that the anomaly has a genetic basis. A number of pathologic conditions which have been observed in association with the osseous deformity of the syndrome are explained in the light of recent observations in the field of experimental embryology.

WINKELMAN, Philadelphia.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

Robert A. Groff, M.D., *Presiding*

Regular Meeting, May 24, 1946

Pneumococcic Meningitis Developing in a Patient Treated with Penicillin.
Dr. Charles S. Kambe (by invitation) and Dr. Robert C. Pope (by invitation).

A case of pneumococcic meningitis with recovery was presented, thought to be of interest because the patient was receiving penicillin in therapeutic doses when the meningitis developed.

L. P., a man aged 49, who had been struck by an automobile, was admitted to the Episcopal Hospital on Feb. 22, 1946, in an unconscious state, with a compound fracture of the right leg and numerous other extensive lacerations, contusions and abrasions.

On his regaining consciousness and after improvement in his general condition, the patient was taken to the operating room, where, with the use of pentothal anesthesia, his wounds were debrided and dressed.

He was given routine postoperative care and treatment for head trauma, with the addition of 200,000 units of penicillin daily, given in doses of 25,000 units by intramuscular injection every three hours, and 100,000 units daily for two days, administered by continuous drip through a sterile catheter into the compound fracture wound.

For three days his condition was good; but on the morning of the fourth day he had a temperature of 104 F., leukocytosis, nuchal rigidity, severe headache and other signs of meningeal irritation. A spinal puncture revealed increased pressure and cloudy fluid, loaded with pneumococci.

Treatment consisted of intravenous and, later, oral administration of sulfadiazine in amounts which kept the blood level close to 20 mg. per hundred cubic centimeters, adequate intake and output of fluids, intramuscular injection of 400,000 units of penicillin daily and repeated spinal punctures, with the administration of 30,000 units of penicillin intrathecally once or twice daily.

The patient's course was especially stormy during the first week. His temperature fluctuated between 102 and 104 F., rectally; the pulse and respiration were rapid and irregular, and during most of this time he was semistuporous. Since the white cell count became normal on the eighth day and cultures of the spinal fluid had been sterile since the second day, all forms of medication were discontinued, on the possibility that they might be responsible for some of the symptoms. Though his condition was much improved the next day, he relapsed in another twenty-four hours and became delirious; so the previous therapy was continued.

It was practically impossible to make the lumbar punctures on this patient without considerable sedation; for this purpose, tribromoethanol solution U. S. P. and pentothal were found most useful. On one occasion, however, the same amount of tribromoethanol solution as that which he had previously tolerated easily produced oversedation, and emergency resuscitative measures had to be employed.

The patient slowly improved and on the seventeenth day seemed so well that the medication was discontinued. Six days later, however, he had a second relapse,

and the previously outlined therapy was again instituted, but with use of sulfamerazine. His further convalescence was essentially uneventful, and he was discharged on April 15, after fifty-two days.

The exact portal of entry was not determined, since cultures of secretions from the wounds and throat were sterile after onset of the meningitis. Attempts to type the pneumococcus were also unsuccessful.

DISCUSSION

DR. A. S. TORNAY: My colleagues presented this case, not to offer another cure of pneumococcic meningitis, but as a case in which meningitis developed during penicillin therapy and an organism sensitive to penicillin was found in the spinal fluid after onset of the meningitis.

A dose of 200,000 units of penicillin daily is as good as, or better than, the average dose used in treatment of most infections with organisms sensitive to the drug. The reason that meningitis developed in this case is not yet clear. I believe I am correct in stating that as yet the mechanism of control of infection in the nervous system with penicillin is not known.

As a result of our experience with this patient, I feel that in cases of cranial trauma with fractures through the frontal sinus, and possibly other parts of the skull, one should use a sulfonamide drug instead of penicillin as a prophylactic measure against the development of bacterial meningitis. In this particular case it was impossible to determine the source of infection. We felt that it was due to direct extension on the basis of trauma, but there was no roentgenologic evidence of fracture of the skull. Several features of the case were of interest during its management.

First, at the beginning of the meningitis itself, considerable difficulty arose because the patient exhibited evidences of increased intracranial pressure about every twelfth hour. Fortunately, regular spinal punctures seemed to control this complication. Another interesting thing about the course of the meningitis was the distinct tendency to relapse. The patient had two relapses during his hospitalization. I believe that for a year other relapses may occur.

I wish to thank Dr. Kambe and Dr. Pope for their excellent care of this patient. I, for one, did not expect him to live.

DR. GEORGE D. GAMMON: Did I understand the authors to say that penicillin was not as good as the sulfonamide drugs in cases of fracture of the frontal sinus?

DR. A. S. TORNAY: As a prophylactic agent in cases of cranial trauma I prefer the sulfonamide drug to penicillin.

DR. GEORGE D. GAMMON: I understood they meant the sulfonamide drugs were superior in treatment.

DR. A. S. TORNAY: No, they did not say that.

DR. GEORGE D. GAMMON: In the discussions at the meeting of the American College of Physicians last week, we were told of cases in which there was early development of resistance to chemotherapeutic agents. I wonder whether there has been any second study of the particular organism in this case to see whether resistance to penicillin had developed.

DR. A. S. TORNAY: On the first spinal tap, and possibly the second, the organism was recovered, but not after that; so no test of sensitivity could be carried out.

DR. ROBERT A. GROFF: This is an interesting subject and raises the question which Dr. Gammon has already asked—whether or not the use of penicillin as a prophylactic drug is dangerous.

From my experience, I should say there is a possibility that by using penicillin prophylactically one is in some instances making the organisms penicillin resistant. For that reason, I wonder whether one is justified in using penicillin prophylactically.

Was I correct in understanding Dr. Kambe to say that the fracture went through the frontal sinus?

DR. CHARLES S. KAMBE: No, there was no fracture of the skull. There was a compound fracture of the leg, but no other fracture.

Coccidioidomycosis: Report of a Fatal Case. DR. C. NELSON DAVIS.

A fatal case of cerebral coccidioidomycosis was reported. The diagnosis was established post mortem. During life the condition was considered to be either tuberculous or syphilitic meningitis, with the remote possibility of its being a torular infection.

Coccidioidomycosis is an endemic disease encountered in the San Joaquin Valley, in southcentral California, southern Arizona, New Mexico and western Texas. Most residents of these areas are infected with the coccidioides, but the infection is of a benign type. About 1 in 500 persons has the progressive form of the disease, which is disabling and usually fatal.

Man is considered to become infected by inhalation of the dust contaminated with the fungus or by entry of the organism through the skin after injury.

REPORT OF CASE

M. E., a Negro aged 27, single, was admitted to the veterans' service of the Philadelphia Naval Hospital on Oct. 19, 1944. He had been in reasonably good health until four months prior to his admission, when headache and a cough developed. These symptoms were progressive at the time of his admission. On admission, he complained further of night sweats, stiffness of the neck and occasional blurred vision. His symptoms persisted and gradually increased in intensity until he died, Jan. 25, 1945. In the final week of his illness he had periods of delirium, and he was in coma during the last forty-eight hours of life.

Neurologic Findings.—There were stiffness and tenderness of the neck. It was not possible to flex the chin on the chest. The pupils were sluggish; the deep reflexes were absent; the margins of the optic disks were blurred, and the left abducent nerve was paralyzed.

Ophthalmologic Study.—Both fundi showed papilledema. The surfaces of the disks were hyperemic, with several small retinal hemorrhages about each disk. The fields were contracted.

Electroencephalographic Readings.—There were some 4 and 6 per second and 8 per second waves throughout both hemispheres.

Laboratory Studies.—The urine was normal; the Kahn reactions of the blood and spinal fluid were negative. The sedimentation rate was 16 to 26 mm. in one hour. The white blood cell count was persistently high; the cell count of the spinal fluid was 280 to 468 per cubic millimeter; the protein of the spinal fluid was never below 100 mg. per hundred cubic centimeters. The spinal fluid pressure was persistently elevated, varying from 410 to 450 mm.

Pathologic Study.—The convolutions of the brain were somewhat flattened, and the sulci were smaller than normal. The pons and the lower part of the cerebellum were matted down with a pale fibrinous exudate. The ventricles were moderately enlarged. The upper cervical portion of the cord was softer than normal.

Histologic study showed an inflammatory reaction, with many large and small circular cells showing a thick refractile capsule. Many of these were within giant cells. These bodies were the spherules of Coccidioides immitis.

DISCUSSION

Dr. H. C. Schlumberger (by invitation): What Dr. Davis said about the importance of this infection particularly from the point of view of the Army, is quite true. The Army Air Forces sent large numbers of men into the endemic areas. There, many of them were exposed to coccidioidomycosis, or San Joaquin Valley fever

It is only fair to stress now that this generalized infection occurs only in about 0.05 per cent of cases of the disease. The generalized form is nearly always fatal. In about 40 per cent there is evidence of involvement of the central nervous system, usually meningitis.

At the Army Institute of Pathology my associates and I have autopsy records in well over 30 cases. In 23 cases the brain had been examined; in 15 there was definite evidence of cerebral involvement. In 13 cases there was meningitis, and in 2 of these there were also small foci in the cerebral cortex. In 2 cases in which there was no meningitis two small granulomas were present in the cerebral parenchyma.

It is interesting that in the cases of generalized infection there is frequently a negative reaction to the cutaneous test, whereas in cases with involvement of the lungs only the reaction is positive.

My colleagues and I had a case at the Valley Forge General Hospital of a soldier who had been stationed in one of the endemic areas. At autopsy, I could not find a focus in the lungs, although I looked for it, knowing that he had coccidioidomycosis.

Dr. Sherman F. Gilpin: If I understood Dr. Davis correctly, I got the impression that it might be difficult clinically to tell this form of meningitis from tuberculous meningitis. I recall that he said that the chloride content was 580 mg. per hundred cubic centimeters. I wonder whether that was on more than one occasion, and whether the value went any lower than that. It is generally accepted that if the chlorides fall to 550 mg. per hundred cubic centimeters, one may make a diagnosis of tuberculous meningitis. Here, the figure was 580 mg., and the cell count, I believe, was consistent with tuberculosis. I should like to have Dr. Davis say a word about that aspect of the case.

Dr. E. Marcovitz: At March Field, Calif., my colleagues and I saw about 200 cases of coccidioidomycosis. Of all that group, there was not a single one in which an infection of the central nervous system developed.

This case presented many signs of tuberculous meningitis. Also, there were signs suggesting greatly increased intracranial pressure, which might conceivably bring up the question of a cerebral tumor.

Long ago at the Neurological Institute I learned that when a case presented signs suggesting both tuberculous meningitis and cerebral tumor, the diagnosis was very likely to be meningitis due to Torula or some other yeast. I think this case corroborates that principle.

Dr. Robert A. Groff: Was this patient's death characteristic of increased intracranial pressure? It seems to me the entire problem was one of increased intracranial pressure.

Dr. C. Nelson Davis: In answer to Dr. Gilpin's question, the value for the chlorides in this case was considered well within the normal range, although ordinarily 600 and 750 mg. is considered the range for chlorides. Dr. Rathmell

might explain that technical difficulty from the laboratory point of view. In conjunction with that finding, we had persistence of the cell count. The cell count did not gradually increase, as one might suspect with meningitis. The chronicity of the disease was also somewhat against a diagnosis of tuberculous meningitis.

I do not know whether or not this man was in an endemic area. His record could not be obtained at this time.

The patient had terminal pneumonia, and there was some infiltration around the vagus nerves. He had increased intracranial pressure and was severely emaciated.

Neurologic Complications of Diphtheritic Neuritis. DR. HERBERT S. GASKILL.

One hundred and forty cases of cutaneous diphtheria were studied in an Army general hospital with which I was associated. Of this group, multiple neuritis developed as a complication in 61, or 43 per cent. This figure for the incidence of neuritis as a complication is not accurate, since selection played a role in the patients admitted to the hospital.

The clinical picture of the multiple neuritis was characterized by its late onset and its slow, insidious development. The neuritis began either with symptoms referable to the cranial nerves, usually blurred vision, or with paresthesias, such as numbness and tingling of the hands and feet. The symptoms of involvement of the cranial nerve commonly lasted from ten to twenty days. They were followed by the sensory symptoms, at first merely paresthesias, but later objective signs of sensory loss involving all modalities—most commonly, diminution of pain and light touch sensibility. The sensory symptoms and signs usually persisted from six to ten weeks. Toward the end of this period evidence of motor involvement appeared in the severest cases. There was loss of the deep reflexes, together with weakness and easy fatigability of the extremities, and in a few cases atrophy of muscles. The motor phenomena generally recovered in about two months. The disease did not always pass through all these stages. The duration of the neuritis in the average case was one hundred days, but there was wide variation in this, depending on the severity of the neuritis.

Examination of the spinal fluid of all these patients disclosed an albuminocytologic dissociation. The increase in the spinal fluid protein was proportional to the severity of the neuritis in most cases.

The early use of diphtheria antitoxin appeared to protect against the development of multiple neuritis. All the patients recovered completely.

DISCUSSION

DR. GEORGE D. GAMMON: Dr. Gaskill has had an unprecedented experience during the war in seeing 140 cases of cutaneous diphtheria with neuritis. The only thing that approaches it is the experience of other observers in this war; Cameron and Muir, in the Near Eastern Theater, had 100 cases or so. The whole experience repeats that which was so beautifully written up by Walshe from his observations in Egypt in the first world war. The same problem is presented today as then: Are these lesions cutaneous diphtheria, or are they something else? What is the proof that these men had cutaneous diphtheria? The second question is: Where did they get the diphtheria? Was there an epidemic of nasal or nasopharyngeal diphtheria in the region at the time? In how many of these men were the ulcers the result of infection from the patient's own throat? What was the carrier rate for the population from which the material was obtained? In what percentage of the cases was Dr. Gaskill able to recover diphtheritic organisms from the ulcers?

I had experience with peripheral neuritis in Italy; Dr. Drayer can comment on that situation, as he was the neuropsychiatric consultant for the Fifth Army. His experience covered a long period and mine a short one. My associates and I saw cutaneous ulcers among the Germans, and we also saw diphtheritic neuritis. None of the ulcers were open at the time; so we were unable to obtain any cultures from the ulcers. The ulcers were punched out; they destroyed the whole skin. They were anesthetic and multiple. I think their incidence was about 30 per cent in the cases of neuritis which we encountered. Whether the lesion was of the same type as that which Dr. Gaskill saw is, of course, a question.

The Germans called them "dirt ulcers," among other things. Some of their men believed they were diphtheritic ulcers, and others thought they were not. Many studies were made in an attempt to prove whether they were diphtheritic or not; only a few gave satisfactory results.

We saw other patients who had had nasopharyngeal diphtheria, and we made the attempt to diagnose the neuritis as diphtheritic on the basis of bacteriologic studies and antitoxin titer of the serum. It is an interesting problem, for the diagnosis of diphtheria in retrospect is a difficult one. In a high percentage of cases the organism disappears from the throat in three weeks; the neuritis develops in six to ten weeks, so that by the time one sees the patient for the neuritis the chance of recovering the organism from the throat is slight.

Major E. B. Schoenbach made studies of the antitoxin level of the blood of these patients. The titer of their antitoxin was low, both for patients with diphtheria and for patients with diphtheritic neuritis. It was low as compared with that for the control population. There was no difference between the group with diphtheria in which neuritis developed and the group in which it did not.

Our efforts to identify the neuritis as diphtheritic from cultures of material from the nose and throat were failures because we saw the patients late and because the carrier rate for diphtheria in the population which we saw was 17 per cent. That is a very high rate. We could not spot a case as one of diphtheritic neuritis by culturing the secretion from the nose or throat or by determining the antitoxin level of the blood.

In making a diagnosis, then, it is necessary to depend on the clinical features of the disease. In diphtheria the paralysis of accommodation is specific. Palatal paralysis occurs with nasopharyngeal infections. I should like to ask Dr. Gaskill how often he saw it in the cases of cutaneous diphtheria. According to Walshe's theory, it should not occur. He looks on the palatal paralysis as due to local spread of toxin along the regional nerves, such as occurs in cases of local tetanus from spread of toxin in the regional nerves.

Another point which should be emphasized is the appearance of an increase in the protein of the spinal fluid in cases of diphtheritic neuritis, with the resultant confusion with the Guillain-Barré syndrome. Guillain was fully aware of this increase. In fact, he wrote an article on it before he published the description of his own syndrome. People like Gaskill and Livengood and Major Joe C. Johnson, in the Italian Theater, assembled data on cases of diphtheritic neuritis in this war which called attention to the older literature by numerous authors, and they expanded the observations. They have a much larger series of cases than the older literature contains.

I do not want to enter into a discussion here as to what constitutes the Guillain-Barré syndrome; that is a moot point. But it is important to realize that in cases of diphtheritic neuritis the protein of the spinal fluid may be elevated. I think that cases have occurred in civilian life in which the condition has been labeled the Guillain-Barré syndrome when it may have been diphtheritic neuritis.

DR. CALVIN S. DRAYER: Polyneuritis presented a problem in the Mediterranean Theater in that we saw a fair number of cases in which we were not at all sure of the etiologic agent. In many of them the picture resembled the Guillain-Barré syndrome, but the possibility of previous diphtheritic infection could not be ruled out. Thanks to Dr. Gammon and Major Schoenbach, we did find certain deficiencies in our laboratory setup. But, as Dr. Gammon has pointed out, we often saw the patient long after the diphtheritic infection had ceased to be in the stage at which the organism could be isolated by any known method.

DR. H. C. SCHLUMBERGER: What Dr. Gammon says about the Germans is of interest, for they were "tearing their hair out" because of the problems presented by diphtheria of all forms along the Eastern Front. Among the complications was one that has not been mentioned today, but which my associates and I saw in our own troops coming from the region where Dr. Gaskill was active. I refer to the cases of cardiac failure in which the patient dies suddenly and no one knows exactly why he died until culture of material taken at autopsy reveals the presence of Corynebacterium diphtheriae. Usually the Germans were able to grow organisms from such ulcers. Apparently, death occurred from heart failure a long time before the peripheral neuritis became manifest.

I had occasion to speak to Schaltenbrandt, a well known German neurologist. Schaltenbrandt told me they had had only 8 cases of the Guillain-Barré syndrome; obviously, then, they were not making the diagnosis of this syndrome in their diphtheritic cases, for they had literally hundreds of the latter along the Eastern Front.

DR. C. NELSON DAVIS: We had 11 cases of this disease, whatever it may be. Dr. Nicholas Klemmer and I reviewed the cases that came in from the South Pacific area, and we could not be certain that the men had diphtheria. There was no proof in cases from the forward areas that diphtheritic bacilli had been cultured successfully. The men did have a sore throat, but they all had been given diphtheria antitoxin combined with sulfanilamide, and it was impossible to tell whether they had diphtheria or not. They presented what may have been the Guillain-Barré syndrome. At least that is what we considered it, although at that time we were calling it toxic myelitis.

DR. CHARLES RUPP: I wonder whether Dr. Gaskill had any experiences with a case in which the antitoxin was given after the neuritic symptoms had appeared; and, if so, what effect, if any, it had on the neuritic symptoms.

DR. B. HERR: Did Dr. Gaskill try to correlate the virulence of organisms in guinea pig inoculations and the severity of the clinical infections?

DR. HERBERT S. GASKILL: I appreciate all the comments of the discussants, and I shall try to answer as briefly as I can.

I do not know where the soldiers contracted diphtheria. Diphtheria is endemic among the natives, for the local English doctors, who had been out there for many years, accepted it as a matter of course that diphtheria should occur. The disease was very different from the form seen in temperate climates. This point was brought out in a paper by Drs. Kern, Norris and others, who were on a hospital ship in the South Pacific. They soon discovered that many men with red, boggy throats, who clinically did not appear to have diphtheria, had the disease.

Let me cite briefly a case which supports this thesis. A medical officer in a forward evacuation hospital in our area was evacuated to our hospital because of a supposed myocardial infarction. He was known to have had a sore throat for two or three weeks before the so-called myocardial infarction developed. After he had been in the hospital several weeks, there developed neurologic signs and symptoms. He said that prior to the onset of the sensory symptoms in his hands he had noted

loss of accommodation. Objectively, neurologic examination revealed hypesthesia to pinprick in the distal segments of the extremities. We became suspicious then that he might have diphtheritic neuritis, for at that time neuritis developed in the first case of cutaneous ulcer.

Over one-half the patients with cutaneous diphtheria were admitted to the hospital at this time. They all came out of one campaign, the North Burma campaign. At that point we had, I think, only 3 cases from which virulent diphtheritic bacilli were cultured. Eventually, when we were sure that the diagnosis was correct, we radioed back to Washington and asked for a special medium to be flown out. We then found that virulent organisms were obtained in about 80 per cent of cases. Since the lesions did not differ clinically, it seemed reasonable to conclude that the organisms were the same in the two series.

Little is known about the carrier rate. It was exceedingly low so far as our hospital personnel were concerned. Few of them contracted diphtheria while taking care of the patients. There was no possibility of making studies on carrier rates in combat troops. The usual story was that the soldier acquired a blister or had a tick bite or insect bite which resulted in a small ulcer; this later became secondarily infected with diphtheritic organsms and finally developed into the chronic indolent ulcer of cutaneous diphtheria.

Palatal paralysis occurred in 7, or 11 per cent, of the cases.

Antitoxin was given after the neuritis began, not because we were trying to treat the neuritis but because Dr. Livengood became convinced that if the antitoxin was given by injecting it around the ulcer the healing of the ulcer was much more rapid.

There was no correlation between virulence of organisms and severity of neuritis. There was certainly no correlation as to the severity or number of ulcers and the severity of the neuritis.

Dr. George D. Gammon: In reply to Dr. Rupp's question: We saw about 3 out of 45 cases of diphtheritic neuritis in which the antitoxin was given late—by that I mean on the tenth, fifteenth or twentieth day afer the beginning of a sore throat; in these cases a severe type of neuritis developed, which seemed to differ from the diphtheritic type. If the patient had neuritis already and if he was given the serum at the time he had the neuritis, the severity of the neuritis was increased promply. In 2 other cases I recall that the antitoxin produced acute serum sickness, with hives and sudden abrupt neuritis with pain, which lasted about a week and cleared up; this was quite different from the diphtheritic picture. I want to point that out to see whether others have had the same experience.

NEW YORK NEUROLOGICAL SOCIETY

Irving H. Pardee, M.D., *President, Presiding*

Regular Meeting, Oct. 1, 1946

Presidential Address: Growth: Humoral and Genetic. Dr. Irving H. Pardee.

Endocrine Manifestations and Their Relation to the Hypothalamus. Dr. Charles Davison.

It is well known that certain endocrine manifestations, such as water, carbohydrate and fat metabolism and gonadotropic functions, which were previously considered to be related primarily to the endocrine system, are at present thought

to be either of hypothalamic origin or under the neural control of the hypothalamus. The association of lesions of the hypothalamus with disturbances in the aforementioned functions has been proved experimentally and clinicopathologically. In some instances it was difficult to determine whether the resulting dysfunction was of purely hypothalamic or hypophysial origin, or of both. For this reason, a number of observers believe these disturbances to be neurohormonal in origin.

It is definitely established that the hypothalamus is in intimate connection with the endocrine system. Of the various connections of the hypothalamus with the endocrine system the best known are (1) the supraopticohypophysial tract, (2) the paraventriculohypophysial tract and, possibly, (3) the tuberohypophysial tract. Evidence for the existence of the last-mentioned tract is not yet entirely satisfactory.

Eleven cases in which necropsy was performed formed the basis of this presentation. There were 10 cases of tumor. Some of these invaded, while others only compressed, the hypothalamus. There were craniopharyngioma (2 cases), angioma (1 case), pituitary adenoma (1 case), suprasellar meningioma (2 cases), neuroepithelioma (1 case), ependymoma (1 case), hemorrhage of the hypothalamus (1 case), metastatic tumor (1 case) and epidemic encephalitis (1 case).

Lesions of the hypothalamus without involvement of the pituitary gland were observed in 6 of the 11 cases (cases 2, 3, 7, 8, 9 and 11), while implication of the hypothalamus and the hypophysis was apparent in 5 cases. The middle and caudal parts of the hypothalamus were more frequently involved than the rostral part.

Neurosurgery of the Parasellar Region. Dr. Jefferson Browder.

Within and arising from structures adjacent to the sella turcica are encountered a great variety of tumors; some of these are neoplasms; others, retention cysts, and an occasional one is a large aneurysmal dilatation of one of the numerous large vessels that normally course by this region. To attempt to discuss all these lesions would take one entirely too far afield. Moreover, in well regulated neurologic clinics, recognition of most of these tumors has become commonplace, and appropriate surgical therapy has more or less been standardized. No longer does the removal of an adenoma of the pituitary gland or a meningioma in the suprasellar or the parasellar region arouse any more interest than is necessary for the assurance of a successful operation. I should like to venture only one comment concerning these two benign tumors. Far too frequently patients harboring such lesions are allowed to delay operation until the lesion has attained enormous size, thus jeopardizing not only life but, equally important, recovery of function of involved neighborhood structures following surgical removal of the tumor. Fortunately, from a diagnostic point of view, many of the meningiomas, as well as the pituitary adenomas, produce characteristic changes in the visual fields; consequently, such alterations in the function of the visual apparatus are sufficient evidence to warrant surgical exploration while the tumor is still relatively small. There are, however, certain types of neoplasms that arise from or secondarily implicate the hypothalamus concerning which surgical therapy is still somewhat controversial. Unfortunately, many of them are malignant, and therefore seldom curable. Occasionally an unexpected successful outcome may follow the removal of a malignant tumor, as the following brief case history attests.

In 1936 a 10 year old girl was admitted to the hospital with the complaint of headache and morning vomiting of three months' duration, unsteadiness of gait for two months, double vision and impairment of memory for one month and recent pronounced diminution of vision. There were lethargy, stiffness of the neck, a high degree of choking of the disk with secondary atrophy of the optic nerve, almost

if not quite complete blindness, weakness of the lateral rectus muscles and moderate ataxia of the extremities of the right side. Babinski's sign was present bilaterally. There was incontinence of urine. Ventriculographic study disclosed a considerable dilatation of the lateral ventricles and absence of air in the third ventricle. At operation the third ventricle was observed to be occupied by a soft, grayish pink tumor, about 3 cm. in diameter. The mass was removed except for what was thought to be a small piece of tumor tissue attached to the left internal cerebral vein. Histologically the tumor was an ependymoblastoma. Convalescence was relatively uneventful. A course of roentgen therapy was given (with a total dose of 2,800 r). Except for almost complete loss of vision, there was satisfactory recovery. The child entered a school for the blind and has made exceptional progress in her studies. In 1945, nine years after operation, she was readmitted to the hospital, and ventriculographic examination disclosed persistent moderate dilatation of both lateral ventricles and a slightly dilated, centrally placed third ventricle. It was concluded that evidence of regrowth of tumor could not be demonstrated.

This history indicates what may be accomplished in exceptional circumstances, especially when one is dealing with an ependymoma. Possibly surgeons have been too conservative in the treatment of slow-growing types of gliomatous tumors. More often, however, the neoplasm is obviously grossly invasive; consequently, an attempt at surgical excision will almost certainly lead to an early death.

In cases of invasive tumors obstructing the flow of cerebrospinal fluid, the establishment of artificial communications between both lateral ventricles and the third ventricle permits the fluid to by-pass the point of block, and useful life may be regained. In several instances, after this procedure, the clinical features representing hypothalamic dysfunction did not become evident for one to three years after operation, whereas in other cases the operation served only to precipitate death or to set up a chain of events that ultimately terminated in death.

The bright side of the picture for all concerned is the group of benign tumors; and once it is established by ventriculographic examination that the lesion is limited to the anterior aspect of the third ventricle, "hope runs high" that the tumor may be a paraphysial cyst, more commonly termed colloid cyst, of the third ventricle. The nature of this lesion need not detain us here, since it has been adequately discussed by Masson, Stookey, Dandy and McLean. It should be pointed out again, however, that the paraphysial cyst should be differentiated from the rarer cyst of the choroid plexus of the third ventricle. The epithelium of the cyst of the choroid plexus is nonciliated and lies on the external aspect of the cyst, whereas in the paraphysial cyst the epithelium is ciliated and lines the lumen of the cyst. In the average case the surgical removal of either type should not be technically difficult; however, care must be exercised to remove the paraphysial cyst totally, lest there be a recurrence.

While all these tumors, that is, chiasmal and hypophysial gliomas, cysts of the third ventricle, suprasellar and parasellar meningiomas, extrasellar extensions of hypophysial growths and others less commonly encountered, may and do functionally disturb the hypothalamus, it is the craniopharyngioma, or tumor of Rathke's pouch, that produces the most striking so-called vegetative disturbances, which are of considerable clinical significance but need no elaboration here. Surgeons have had the added opportunity to observe accentuation of abnormalities in vegetative features after attempts at total removal of either cystic or solid suprasellar craniopharyngiomas. Notably, there are pronounced tachycardia, arterial hypotension, mottling of the skin of the extremities, hyperthermia, diabetes insipidus

and, most striking of all, an alteration in consciousness, the state ranging from what appears as a peaceful sleep to obvious profound coma. In my experience, this somnolent state has persisted in some cases as long as eight days, occasionally terminating abruptly and the patient awakening in a manner simulating the springtime arousing of the hibernating animal.

Besides the problem of the clinicopathologic alterations produced by a craniopharyngioma, changes which have been thoroughly elaborated by many authors, there remains the unsolved question of satisfactory therapy for a lesion that in the majority of instances seems to be of a benign character. Surgeons, in particular, have been guilty of reporting a patient as cured from whom a craniopharyngioma has been removed, even though only two or three years has elapsed since operation. Simple aspiration of a cyst will at times result in cessation of symptoms for a comparable period; yet no one should hold that this procedure is more than a makeshift. From his vast experience, Cushing concluded that unless the lesion could be destroyed or inactivated in situ the mortality would doubtless remain high. Globus and others have noted that when the floor of the third ventricle and regional structures are grossly displaced they are commonly firmly adherent to the surface of the tumor. While some craniopharyngiomas are solid, the so-called adamantinoma, they are more often cystic. Of necessity, the only method of dealing with the solid tumors is excision, even though the procedure carries a high mortality. Some of the more commonly encountered cysts may be successfully treated by establishing a pathway for drainage between the cyst and the cerebral ventricular system, as advocated by Scarff. An alternate method of draining away the fluid elaborated by the inner lining of the cyst is excision of a part of the frontal lobe of the brain and drawing a part of the wall of the open cyst into the ventricular cavity. Any fluid elaborated by the epithelial surface of the cyst may be discharged into the cavity. Subsequently, if indicated, the cavity resulting from excision of the frontal lobe may be tapped and its fluid contents aspirated without fear of damaging cerebral structures.

DISCUSSION OF PAPERS BY DRS. PARDEE, DAVISON AND BROWDER

DR. WALTER TIMME: I remember that years ago, generations ago, practically the same discussion on the relation of the hypophysis and the hypothalamus was presented before this society as we have had this evening; I do not know whether there has been any progress in this field; it seems to me that the basis for discussion is still exactly the same. I wish particularly to speak of Dr. Pardee's address, which was of encyclopedic proportions. He discussed practically every type of growth function and dysfunction we have ever known, and the work of accumulating that material must have been tremendous. I congratulate him on the type and amount of work which he has accomplished. Some of the cases he presented are of the type we have discussed many times heretofore, and some are not. Some cases are interesting because of the difficulty of showing why; even with open epiphyses, growth cannot be produced to any extent. It has formerly been thought that with open epiphysial lines in the long bones utilization of the growth hormone of the anterior lobe of the pituitary was enough to stimulate growth materially. That is not so. Why is it not so? Many reasons can be proposed, but most of them are wrong; one of the most important is the antagonism of the pineal gland to the pituitary, and the pineal gland itself inhibits growth. One almost never takes into consideration the effect of the pineal body when presenting patients with lesions of the anterior lobe of the pituitary gland. That was brought out in a neurologic meeting two or three years ago by Loyal Davis,

of Chicago. He had done work on tumors of the pineal body and recognized the fact that some children began to grow after removal of a tumor of the pineal body, and he did not know why. The reason was the removal of inhibition of the pituitary gland. There is another reason. Secretions and extracts of the pineal body have an actual effect in reducing the speed of most growths. I have used such preparations successfully for that purpose, as in slowing the growth of the cancer cell; of course, it does not cure the cancer. Therefore, one must take into consideration such factors as the pineal gland when it is found impossible to produce growth by using preparations of the anterior lobe of the pituitary. It is sometimes impossible to determine the importance of the pineal gland; there is no way of measuring the effect of the gland except to assume it as a reason for inability to produce growth.

There is another point about the growth hormone of the anterior lobe. Riddle and Evans, of California, differed regarding the effects of prolactin (lactogenic hormone of the anterior lobe of the pituitary), described by Riddle who expressed the belief that this principle is the same as the growth hormone of the anterior lobe and produced growth by using the substance. Why? Prolactin has the effect of stimulating the mammary glands and producing by such stimulation a cessation of ovarian function, so that massive and intense hemorrhages, lasting for weeks and responding to no other treatment, will nearly cease after a few doses of prolactin. The effect is almost miraculous. The very fact that prolactin produces a negative disturbance in the gonads would indicate, as a corollary, that it would produce an increase of growth, for when the gonads are deficient growth proceeds more rapidly.

I am glad that Dr. Pardee mentioned the thymus gland as a factor in growth. The thymus gland is certainly the basis of accretion in the body. There is, for example, the accretion of bone. As Dr. Pardee mentioned, Rowntree showed in successive generations of his rats that feeding the animals thymus produced increased growth in their descendants. As a corollary of that observation, given a giant with a very small pituitary gland, the size of a pea perhaps, but with abnormally continuing growth, that growth may be stopped very rapidly by subjecting the thymus to roentgen radiation. In this case, it was the thymus that produced his gigantism, not the pituitary. Most of the long-legged giants have hypopituitarism, not hyperpituitarism. The growth is a thymic growth, as Dr. Pardee brought out.

The achondroplastic dwarfs are highly interesting. Most textbooks and most authorities declare that nothing can be done to overcome the achondroplasia. In nanism the legs are entirely too short and the upper part of the body is normal; and it is said that the deformity is congenital and nothing can be done about it. I had a young girl (brought to me by Dr. D. S. Bayard, of this city, a pediatrician), who appeared like a penguin at the age of 1½ years. One could see only feet coming from below her little skirt; there were practically no legs to speak of. The prognosis was poor, but on presentation of the anterior lobe of the pituitary gland with some thyroid and calcium the girl grew both in intelligence and in height until she became a normal child, with a torso-leg ratio which was normal. The legs grew out of all proportion to the torso, and she became so normal, in fact, that she graduated from college, although that may not necessarily mean normality.

As for the Lorain dwarfs (persons with dwarfism and infantilism), they are almost perfect specimens of humanity, but small, and I have never been able to improve their height or stature. They are practically always normal in intelli-

gence, or even quick-witted, but nothing can be done regarding their height, as can be done with the achondroplastic dwarf.

I wish to congratulate Dr. Pardee on this useful presentation of the various anomalies of growth.

Dr. Davison's paper was highly complex. The relationship of the hypothalamus to the hypophysis and the other centers is so complicated that even with the most painstaking operative procedures one cannot be sure what one has done. I talked personally with Roussy; he expressed the idea that the hypophysis could be ablated without any effect on adiposity. I think Dr. Davison made a statement of that kind this evening. As a matter of fact, the ablation of the hypophysis was not complete, but left a certain number of pavement cells intact, and it is these pavement cells which have to do with adiposity; when these pavement cells are removed, adiposity results. These pavement cells are probably related to the cells of the tuber cinereum.

One of the important relationships of the hypothalamus to the hypophysis is that which exists between the mamillary body and the cortex. This relationship may produce the somnolence that frequently accompanies hypothalamic disturbances.

This summary shows my attitude toward what is being attempted in the field of hypophysial disturbances. The work that is done in the laboratory on hypophysial material must be checked and rechecked before any valid conclusions can be drawn.

DR. LEO M. DAVIDOFF: I shall confine my comments to the discussion of Dr. Browder's paper. Dr. Browder summarized the problem of the neurosurgeon, and he did it so well in the short time which he had that it would be ungrateful to add anything to what he had to say, for it would be taking advantage of the fact that he did not have time to say it. I should like only to state that recently I have changed my surgical approach to the colloid cyst, and also to the craniopharyngioma, in that I no longer make a transcortical incision into the ventricle but separate the two hemispheres of the brain and incise through the corpus callosum. The reason for this is that in cases in which a colloid cyst is approached through the cortex the patient sometimes has postoperative epilepsy. This is a distressing after-effect in a case in which the cyst has been removed successfully. With the trans-corpus-callosum approach one can avoid that difficulty. Another advantage is that, instead of approaching the foramen of Monro at an angle, one comes down on it directly, so that it is more easily brought into view.

With regard to the treatment of craniopharyngioma by removal of the frontal lobe and draining the open cyst into the cavity, I think Dr. Browder invented this operation, and it is an extremely useful one in certain circumstances, when the cyst is large and the walls of the cyst are adherent so that the tumor cannot be removed. It is sometimes life saving to be able to retap the cyst through the intact skull, and this method presents an opportunity for so doing, and doing it safely. Many methods have been invented for tapping the cyst through a previous trephine opening, but all of them are unsafe except in circumstances like this, in which the only thing between one and the cavity is a little scalp tissue.

In removing a craniopharyngioma completely there is not only the danger of injury to the hypothalamus but, as sometimes occurs, and occurred in a case of mine recently, the possibility of trauma to the optic nerves themselves. In this case, the patient, who was relieved entirely of his tumor, and cured from that point of view except for a slight degree of diabetes insipidus, was free from any serious endocrine disturbances but had reduction in vision. At first he was completely amaurotic, and now is able to see only shadows—a distressing result. In

approaching these histologically benign, but technically often difficult, lesions, the neurosurgeon must keep in mind the possibility of such an accident. It may be worth while to remember, too, that the late Dr. Frazier demonstrated in a series of cases of craniopharyngioma that the secretory activity of the cyst may be diminished, and sometimes completely destroyed, by the use of roentgen radiation; whether or not the actual destruction of the cyst takes place by this means is not certain, because some of these cysts seem to be discouraged in their fluid-forming tendencies simply by partial removal of the wall; nevertheless, from experience in a series of cases, it seems to me that roentgen therapy is helpful; therefore, when a cyst is not completely removed, it may be worth while to give the patient radiation therapy.

Dr. John E. Scarff: I have enjoyed these papers very much. I have two minor personal observations to contribute to the discussion. First, it is common knowledge among surgeons that complete removal of the pituitary gland and the contents of the pituitary fossa is practically never accomplished at operation, but in 1 case in my experience it did seem that at the end of the procedure, owing to the favorable configuration of bone, one could see actually the floor of the sella turcica, which was quite smooth, and that all glandular tissue had been removed. In this case the symptoms were unusual, and I should like to report them, without comment or deduction from them. The patient, whose principal difficulty, and only presenting complaint at the time of operation, had been referable to the optic nerve, exhibited the following symptoms after operation: First, he began to age; he actually seemed to shrivel up. Second, his body temperature fell, so that in the midst of summer he would be seen sitting in the clinic wearing an overcoat and a woolen muffler, actually shivering, and his body temperature would be 94 or 95 F. Third, he was subject to terrific cramps, which came on paroxysmally, involving various muscle groups. On one occasion I was reached on the telephone by a house officer at the patient's request. The patient at that time was in the anesthesia room of a hospital and was about to be operated on for a presumed "acute abdomen." I went at once to see him. He had intense spasms of the abdominal muscles, but I had seen similar spasms before, and I persuaded the surgeon to delay his operation. This the surgeon did, and the muscle cramps disappeared. This patient was thoroughly studied from many angles.

A second personal observation, in this case in connection with the hypothalamus, may be of interest. Several years ago Dr. Stookey and I devised an operation for the relief of obstructive hydrocephalus. This involved the passing of the instrument through the anterior wall of the third ventricle and on, posteriorly, through the floor of the third ventricle, in the region of the tuber cinereum and the mamillary body, leaving an opening 0.5 cm. in diameter through these structures, connecting the third ventricle with the interpeduncular cistern. The first time we did this operation we anticipated a serious disturbance in water metabolism, but none occurred. We have now performed this operation on approximately 20 patients without producing diabetes insipidus, even temporarily, in any of them.

Dr. Joseph H. Globus: Dr. Pardee has already given us a foretaste of what we are to expect for the rest of this term. Above all is his promise to complete sessions by 10:30 p. m., leaving me but a few minutes for the few remarks which I shall make. He has also demonstrated his ability to present highly instructive material and to provide us with an interesting program.

Dr. Davison has demonstrated in a convincing way something with which we are familiar, namely, that the hypothalamus has an important influence on endocrine

functions. He presented a large number of cases, all with massive lesions in the hypothalamic region, either neoplastic or resulting from such growths. I should have liked to see more restricted lesions, so that correlation of the site of the lesion with the actual disturbance in function could be made with greater accuracy. The massive lesions demonstrated here have involved almost the entire hypothalamus, and the question arises whether they have not influenced other structures in the neighborhood of the hypothalamus. The demonstration has left the subject open once more, so that in another twenty years we shall probably have a program on the hypothalamus and then, let us hope, a similar study, but one which, by means of serial sections, may lead to careful correlation of the lesions thus observed and the manifestations presented by the patients under study.

Dr. Davison stated, with regard to polyuria and polydipsia, that he found only 1 case of craniopharyngioma in which diabetes insipidus occurred preoperatively. I have a collection of 15 craniopharyngiomas, and in almost two thirds of the cases diabetes insipidus was present preoperatively. In some it appeared after operation. In cases in which it was present before the operation it disappeared shortly afterward, to recur in some instances at a later date.

There is little I can say about Dr. Browder's paper except in praise, and that I have learned much from it about the way in which tumors in this dangerous situation can be approached.

DR. CHARLES DAVISON: I appreciate Dr. Globus' discussion. I am extremely sorry to disagree with him, but in most of the cases in my series the tumor was fairly well localized to the hypothalamus. I have emphasized that it is difficult to draw conclusions as to which part of the hypothalamus is involved; that of course is not my fault. In 5 of these cases the region was studied by serial sections.

With reference to the craniopharyngioma, I am sorry that I was misunderstood. I said that in a number of the cases of craniopharyngiomas polyuria and polydipsia occurred after operation. I cited the 1 case for this reason.

News and Comment

THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The following candidates were certified at a meeting of the Board in Chicago, Oct. 27 to 28, 1947:

Psychiatry.—By Examination: Albert Ackerman, Washington, D. C.; Edward T. Adelson, Newark, N. J.; Charles Carter Ault, Little Rock, Ark.; * Ruth I. Barnard, Topeka, Kan.; Edward R. Bennett, Staten Island, N. Y.; Murray Bergman, Newark. N. J.; Morris Binder, Northport, N. Y.; Aaron Harry Braverman, Bedford, Mass.; Elizabeth Lynn Bryan, Brooklyn; Allen W. Byrnes, Richland, Mich.; Ralph J. Carotenuto, Brooklyn; Abraham H. Center, Savannah, Ga.; Michael Chaplik, New York; Newman Cohen, Boston; Ernani D'Angelo, Jamaica, N. Y.; John A. Doering, Farnhurst, Del.; John Morris Dorsey, Detroit; Thomas Joseph Dredge, Greystone Park, N. J.; Raphael H. Durante, Philadelphia; Arnold H Eichert, Sykesville, Md.; Benjamin B. Faguet, San Francisco; David M. Ferber, Brooklyn; Louis M. Foltz, Louisville, Ky.; Thomas Holland Fox, Fort Meade, S. D.; William Hanna Gallagher, Traverse City, Mich.; Harry M. Gardiner, Harding, Mass.; Simon L. Goldfarb, Hartford, Conn.; Walter Goldfarb, New York; Michael O. A. Grassi, Philadelphia; Sydney H. Green, Corte Madera, Calif.; Philip Samuel Greenbaum, Tucson, Ariz.; William Stone Hall, Columbia, S. C.; Isidore Holden, Los Angeles; Charles O. Holder, Kalamazoo, Mich.; Mansell B. Holmes, Tuscaloosa, Ala.; Frank J. Imburgia, Parma Heights, Ohio; Walter O. Jahrreiss, Baltimore; Simon Overton Johnson, Lakin, W. Va.; Ernest Frederick Jones, Marion, Ind.; Louis Kaplan, Philadelphia; Saul Howard Karlen, New York; Kenneth M. Kelley, San Francisco; Robert Coleman Longan Jr., Richmond, Va.; William H. Lyons, Detroit; Joseph Marcovitch, Marion, Ind.; Oswald John McKendree, Utica, N. Y.; Sol Brown McLendon, Columbia, S. C.; Edward Ray Miller, Beverly Hills, Calif.; John D'Arcy Morgan, American Lake, Wash.; James M. Murphy, Willard, N. Y.; Elsie S. Neustadt, Quincy, Mass.; John Joseph O'Connell, Ontario, Canada; Robert P. Odenwald, Suffern, N. Y.; William D. O'Gorman, Omaha; Albert Lamoin Olsen, Fort Custer, Mich.; Helen Joyce Perrin, Des Moines, Iowa; Max J. Primakow, Wood, Wis.; Charles Prudhomme, Washington, D. C.; Charles R. Rayburn, Norman, Okla.; Irving Salan, Orangeburg, N. Y.; Louis Schlan, Chicago; Henry Z. Shelton, Orangeburg, N. Y.; Roy C. Sloan, Lubbock, Texas; Willie Mary Stephens, Chicago; Nina Toll, Middletown, Conn.; Clarence A. Vallee, Batavia, N. Y.; Comdr. Robert Lowell Wagner (MC), U. S. N.; David Michael Wayne, Fort Meade, S. D.; Joseph E. Weber, Milwaukee; Paul Wenger, Bedford, Mass.; Mabel G. Wilkin, Bethesda, Md.; * Emil Guenther Winkler, Long Island, N. Y.; Joseph A. Winn, New York; Robert L. Worthington, Topeka, Kan.; Bernard Yood, Boston.

Psychiatry.—On Record: Anthony Trevisano, Castle Point, N. Y.

Neurology.—By Examination: Ernest A. Burrows, Providence, R. I.; * Carl M. Epstein, Topeka, Kan.; * Samuel Futterman, Los Angeles; John William Magladery, Baltimore; Lewis Alan Roberts, New York; John Hallman Taeffner, Philadelphia; Samuel Wood Weaver, Santa Ana, Calif.

Neurology and Psychiatry.—By Examination: Raymond L. Osborne, New York; John Leopold Simon, New York; Miguel Steinberg, New York.

* Denotes complementary certification.

Book Reviews

Mental Mischief and Emotional Conflicts (Psychiatry and Psychology in Plain English). By William S. Sadler, M.D. Price, $6. Pp. 396. St. Louis: C. V. Mosby Company, 1947.

This book was written for the "average" person who wants to know more about emotional conflicts—most likely his own. It is an excellent idea, but the author runs into the same difficulty that all technical writers do in attempting to simplify complicated mechanisms. The result is either an oversimplification or an incomprehensible hodgepodge. This book suffers from being both. There are passages which are simplified enough to make them interesting, but which, unfortunately, strain the facts. There are also long and detailed classifications which the technical reader would have to classify as original but meaningless.

The book tends mostly toward description, and only chapter headings indicate the dynamic aspect. The author describes the illnesses very well, but when he begins to explain the basic origins of the disorders he becomes once more descriptive and not very helpful.

This book was read with the purpose of evaluating its usefulness to the average reader. If an average reader wants to go through 372 pages of purely descriptive material, he is not an average reader. With such a seductive title, the reader is entitled to a better and clearer study of mental illness.

Diseases of the Nervous System. By F. M. R. Walshe, M.D. Price, $4.50. Pp. 351. Baltimore: Williams & Wilkins Company, 1947.

This short, simple text has gone through five editions in six years. This in itself is evidence of a need for such a book. The author has held it deliberately on a practical level, omitting all procedures and considerations not accessible to the practicing physician. As much as the wisdom of the clinical approach to a clinical field is to be admitted, the reviewer cannot help feeling that the author carries it to a point of condescension toward his readers. Might not the practicing physician like to be shown new lines of thought, even though he cannot test them with his own tools? The brief chapter on the psychoneuroses is inadequate.

The Engrammes of Psychiatry. By J. M. Nielsen, M.D., and George N. Thompson Jr., M.D. Price, $6.75. Pp. XIX, plus 509, with 28 illustrations. Springfield, Ill.: Charles C Thomas, Publisher, 1947.

This textbook presents a system of biologic psychiatry. The authors are seeking the engram patterns which underlie human behavior. In the anatomic and physiologic introduction (chapter I), they state that for the functional activities of conation, consciousness, instincts, will, cognition, personality and emotions, one must recognize (*a*) a brain stem component, (*b*) a diencephalic component and (*c*) one or more cortical components. Thus, conation, which is defined by the authors as the tendency to move and is considered by them to be the most fundamental of all cerebral functions, depends on a motor mechanism made up of three levels of cerebral structures: (*a*) the periaqueductal gray matter, (*b*) the ventrolateral nucleus of the thalamus and (*c*) the precentral and postcentral rolandic area (chapter II). A lesion in the periaqueductal gray matter will render the patient devoid of desire to move.

For the complete functioning of consciousness, there exists, likewise, a neuronal system involving the brain stem, the diencephalon and the cerebral cortex (chapter III). A crude form of consciousness is mediated by the brain stem and the diencephalon. The engram system, which is essential to crude consciousness, is located

at the junction of the mesencephalon, the subthalamus and the hypothalamus. Lesions of the thalamus cause loss of attention, i. e., loss of the capacity to focus awareness.

Those instincts which are present at birth have their neuronal patterns in the diencephalon and the brain stem (chapter IV). These instincts are: crying; sucking; defensive reaction against falling; holding the breath and bearing down in evacuation of the bowels and bladder; turning the head and eyes in response to light and sound, and response to coddling. Instincts which require perception, recognition and organized concepts for their execution require also the cerebral cortex. Emotion is described as the result of the facilitation or the impediment of an instinctive drive and is expressed fundamentally by engrams in the hypothalamus (chapter V).

The authors define personality as the habitual reaction patterns of the person (chapter VII). The engrams of personality also have a brain stem, a diencephalic and a cortical component. The cortical site of lesions causing change in personality is primarily in the cingulate gyrus—frontal lobe engrams, and in the case of the frontal lobes chiefly in the orbital cortex. The functions of perception, recognition and recall are, with one exception, cortical functions in man (chapter VIII). The exception is man's capability of crude perception of touch and pain without the cortex.

Psychoneuroses are defined as mental mechanisms of defense and represent partial failures (and necessarily partial successes) in meeting frustrations (chapter XII). A psychoneurosis is an unconscious confession of defeat in one sphere of activity but with preservation of the personality as a whole. The authors believe that the psychoneurotic and the psychopathic personality are incompatible (chapter XIX). The pathognomonic sign of the psychopathic personality is the failure or inability to make practical use of the concept of time.

The basic pathologic feature of schizophrenia, the authors postulate, is an engrammatic disorganization of the diencephalon (chapter XI). This is indicated by the early symptoms of apathy, emotional paucity and loss of interest and attention. As the schizophrenic process continues the cortical functions become implicated. The symptoms found in manic-depressive psychosis are related to the level of activity of the diencephalon (chapter XVI). In the depressed phase of the illness there is a depressed (but not disorganized) function of the diencephalon. In the manic phase, on the contrary, the diencephalon is stimulated. The authors postulate that in the involutional psychosis there is a partial diencephalic disorganization along with endocrinal involution (chapter XVII). Paranoia is considered to be the psychotic rationalization of failure in the predisposed person (chapter XVIII).

This book reflects the extensive interest and experience of the authors in problems of the pathologic physiology of the brain in relation to disturbances in mental functioning and behavior. The authors are expounding, as they see it, the anatomic and physiologic substratum of psychiatry. They have presented the existing evidence, both experimental and clinicopathologic, from their work and that of others in support of their hypotheses. They are aware of the gaps in the present knowledge of the subject. Much of what they present is tentative and subject to later revision. The book is stimulating and is bound to give rise to controversy. It will be criticized by some for its lack of approach from the standpoint of Gestalt psychology.

The style of writing is refreshing and readable. Case histories are well chosen. The book contains much practical information for the practicing psychiatrist and the psychiatric student. The book is well indexed and well illustrated and contains a bibliography of the works cited.